3D Bio-MEMS device to detect Salmonella Bacteria

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OUTLINE

- General Concepts
- Examples of Micro-systems
- Summary

- LiGA
- Lithography; X-ray masks
- Exposures
- Electroplating; Hot-embossing

- Detection of Salmonella Bacteria
- Biological Protocol
- Devices and Tests
- Conclusions

Miniaturization

By miniaturizing applications you can...

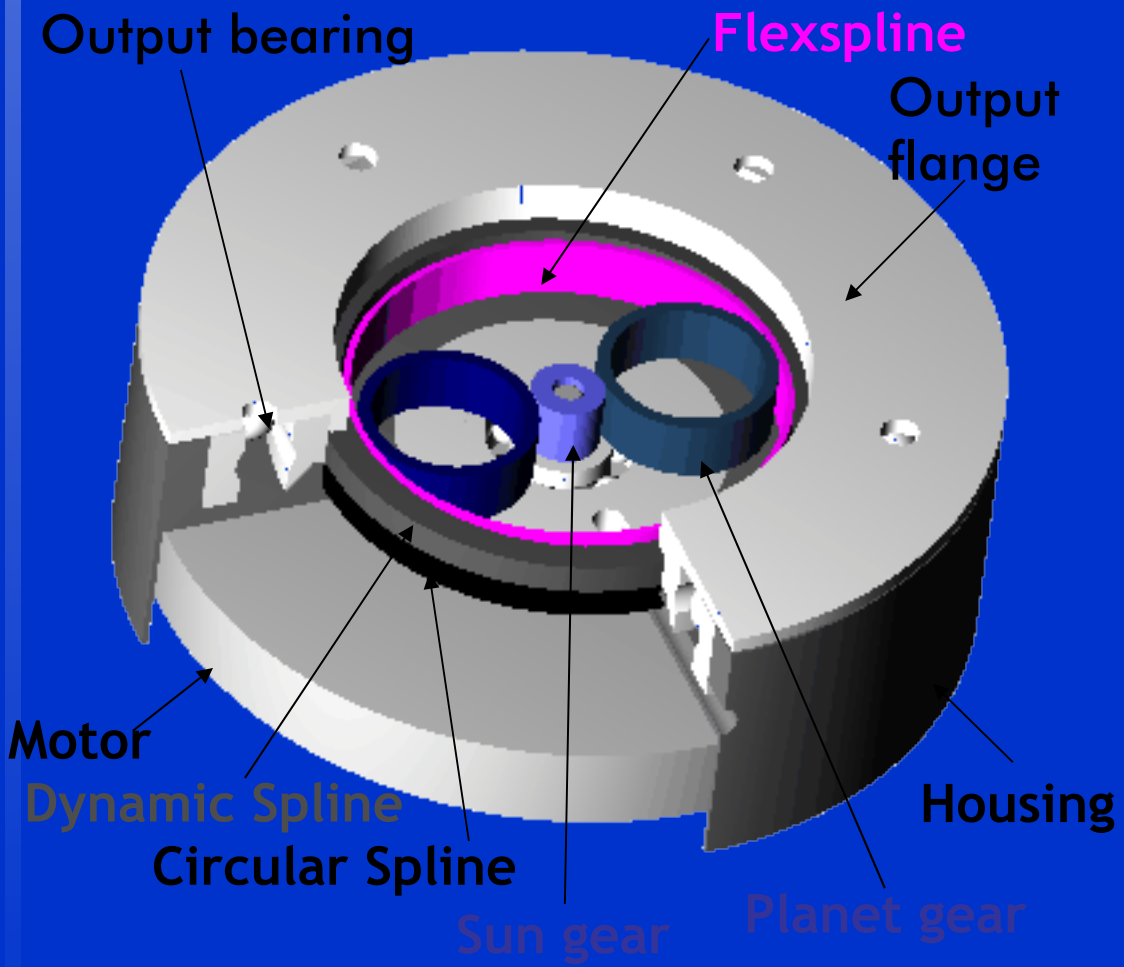
- **enhance performance and productivity**
- **reduce sample and reagent consumption**
- **work more easily with nanoliter sample volumes**

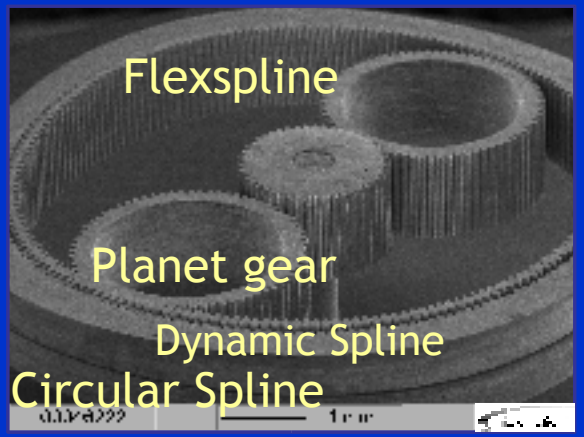
Integration

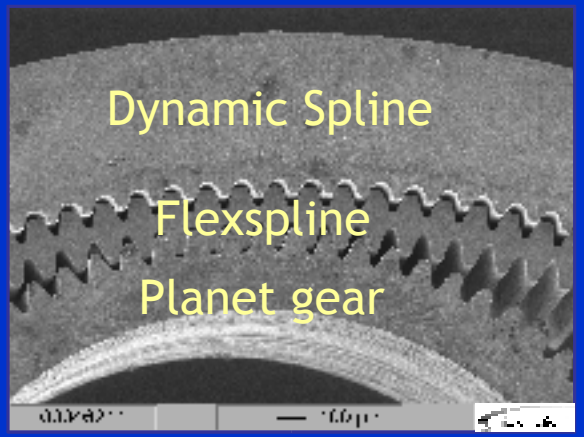
By integrating multiple steps into a single streamlined process you can...

- **increase productivity**
- **improve reproducibility**
- **eliminate the need for user intervention**
- **minimize the risk of losing samples**

Micro Harmonic Drive® Gear







Advantages

- **Zero backlash yet miniature dimensions**
- **Excellent repeatability**
- **High torque capacity**
- **High reduction ratios with 6 parts**
- **High efficiency**
- **Extremely flat design**
- **Very low weight**

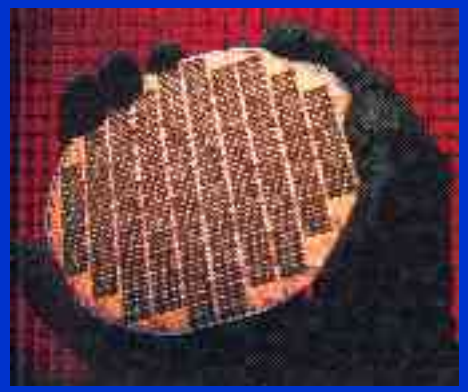
Applications for Micro-Motors

Medical Equipment

Optical Communication

Laser Equipment

Measuring Machines



Semicon

Robotics

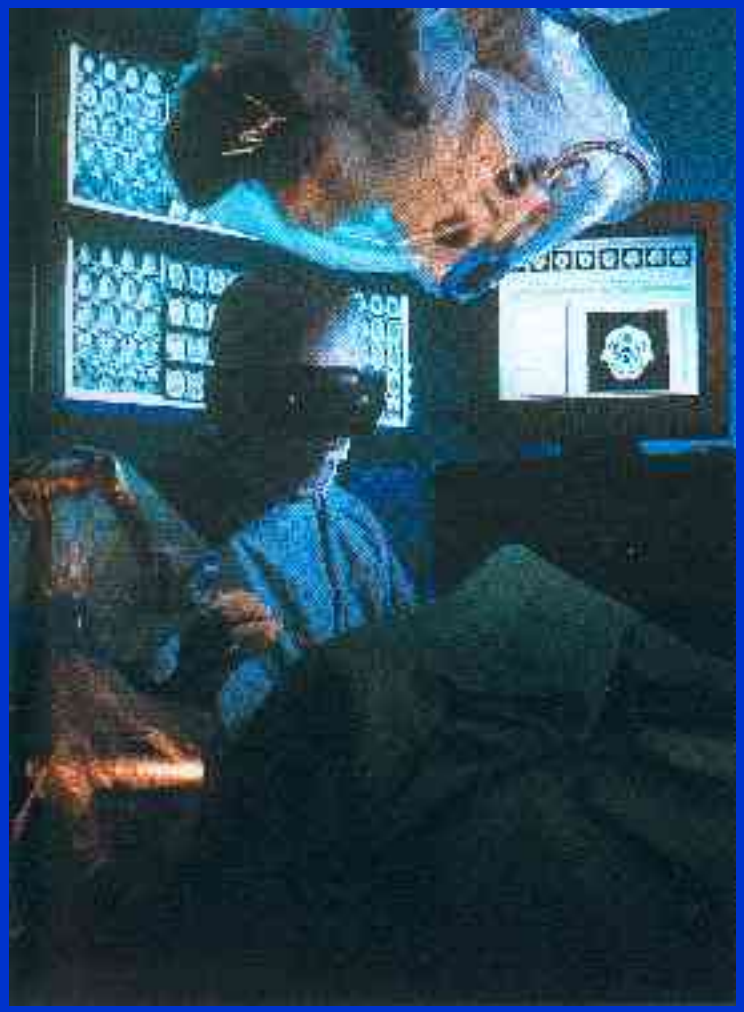
Microscopes

Biotechnology

Spacecraft

Aircraft

Bio-MEMS



Biotechnology

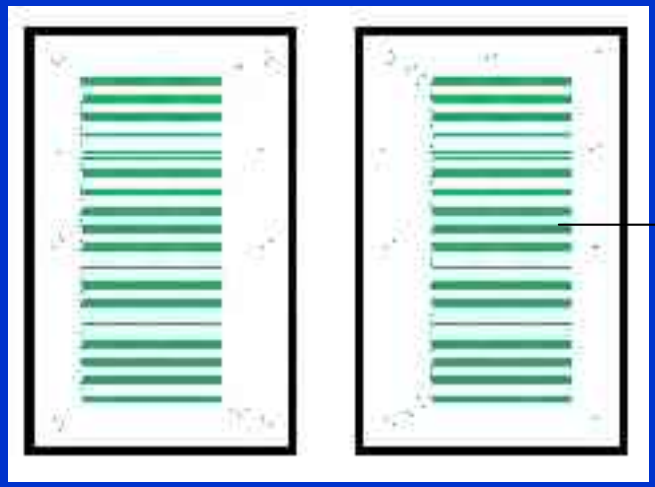
Medical Equipment

Microfluidics

Microfluidics: Walking on Water...

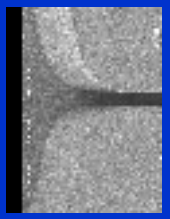
High Aspect Ratio μ-GC

Gas Chromatograph - Drawing Board to Plastic Microstructures

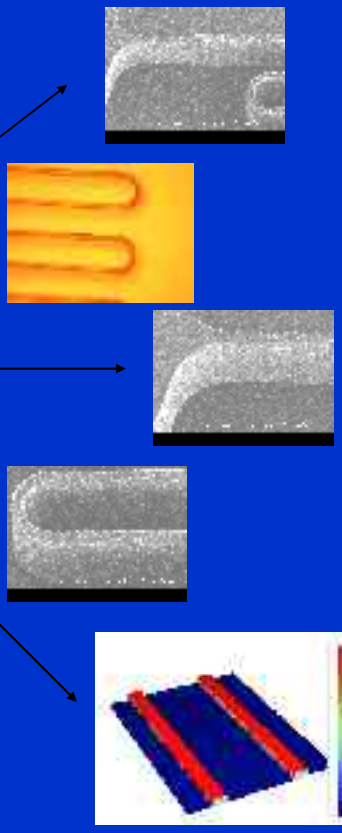


Drawing of a micro gas chromatograph (GC)

Nickel GC mold insert fabricated using LIGA

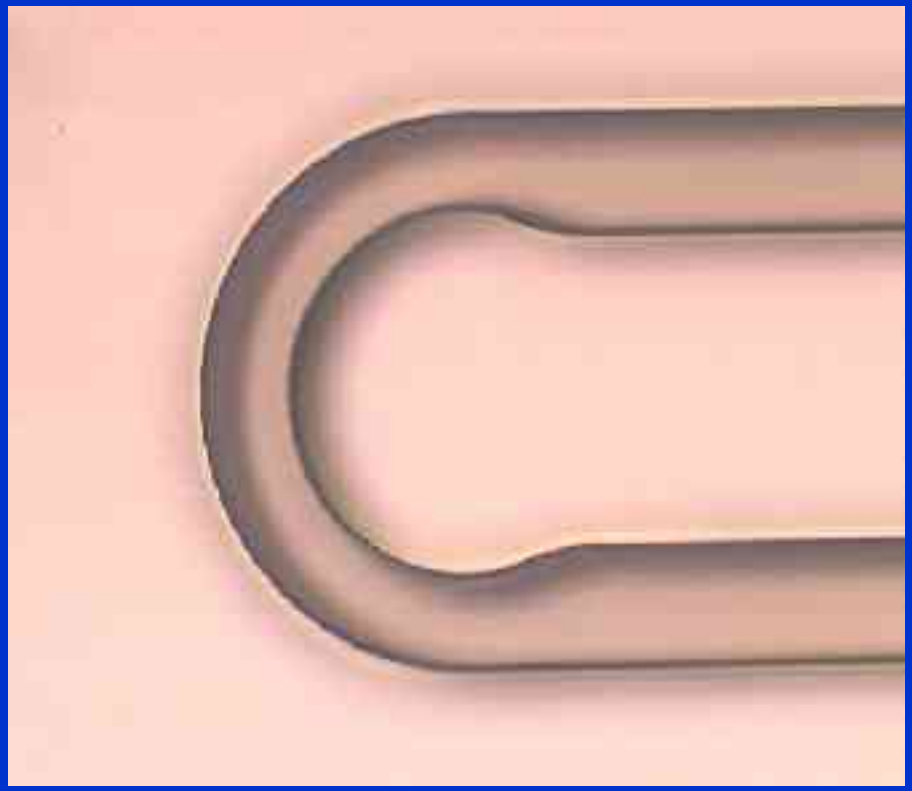


SEM picture of a small section of the nickel micro GC mold insert

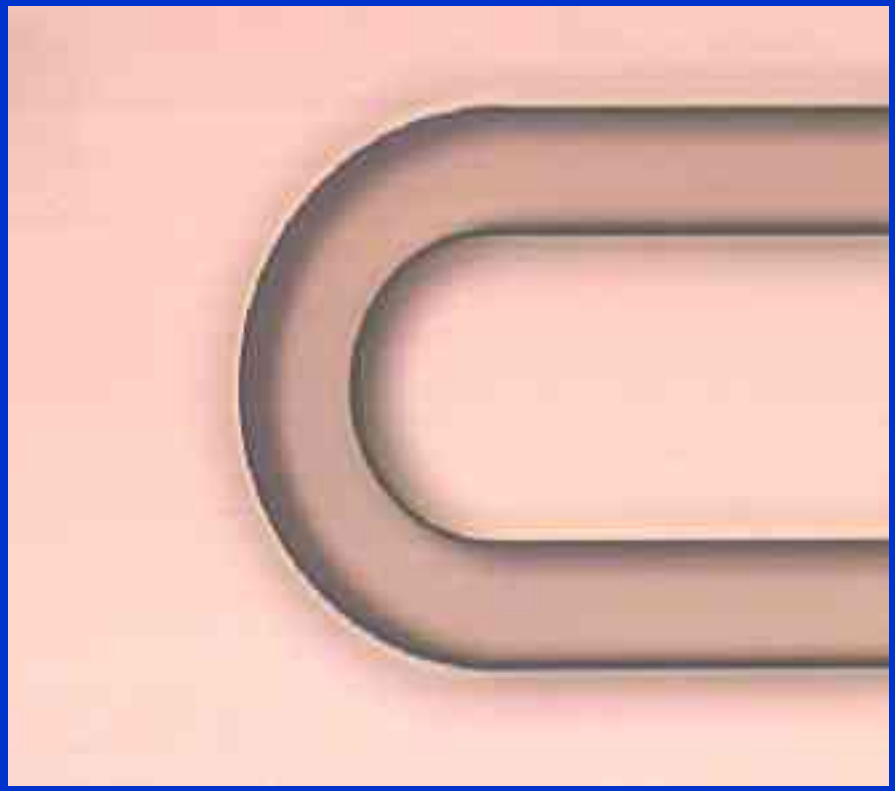


Microstructures molded in plastic using LIGA fabricated GC mold tool. The SEM pictures show various sections. These structures are 50 microns wide and 420 microns high.

Some examples

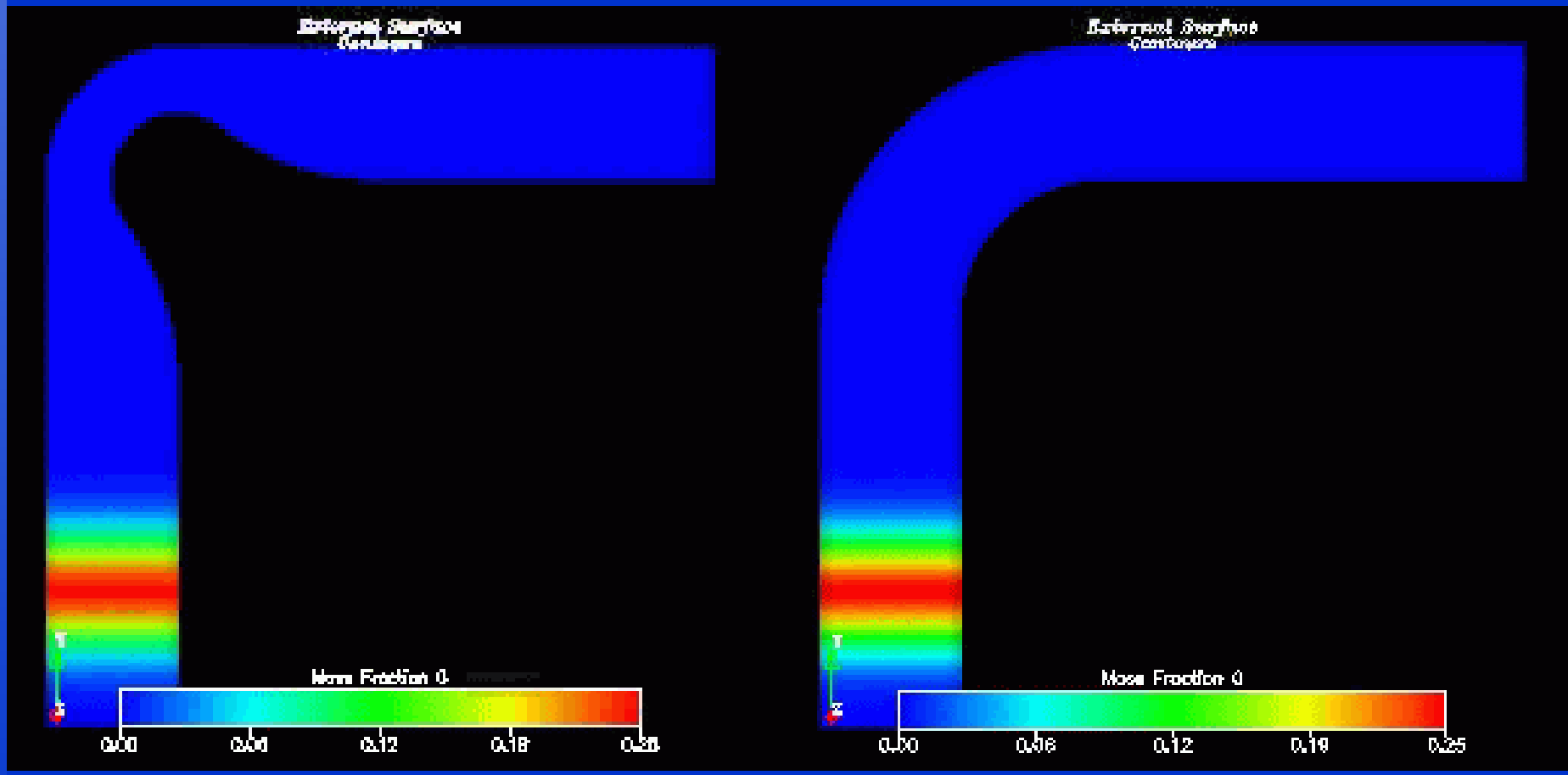


thickness = 500 microns;
column diameter = 100 microns;
turn diameter = 75 microns



thickness = 500 microns;
column diameter = 100 microns;
turn diameter = 100 microns

GC


Mass Fraction 0
0.00
0.06
0.12
0.18
0.25
Mass Fraction 0
0.00
0.06
0.12
0.19
0.25

Summary

Microfluidic lab-on-a-chip technology represents a revolution in laboratory experimentation.

It combines manufacturing methods from the microchip industry with expertise in fluid dynamics, biochemistry and software and hardware engineering to develop miniature, integrated biochemical processing platforms, systems, and instrumentation.

The benefits of miniaturization, integration and automation will strengthen research-based industries and may also lead to new point-of-care medical and analytical devices.

To keep in mind !

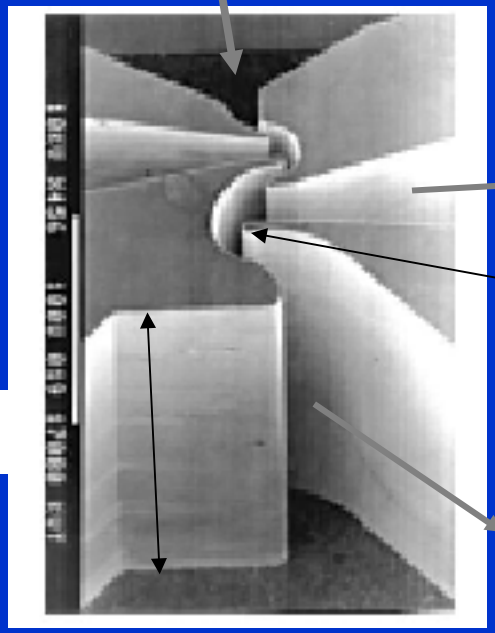
- **Let technology NOT drive you towards complete miniaturization at the start !**
- **Stay focused to fabricate a product !**
- **Develop strategic partnerships !**
- **Establish a multi-disciplinary TEAM effort !**

The beginning …

Late 70's/early 80's

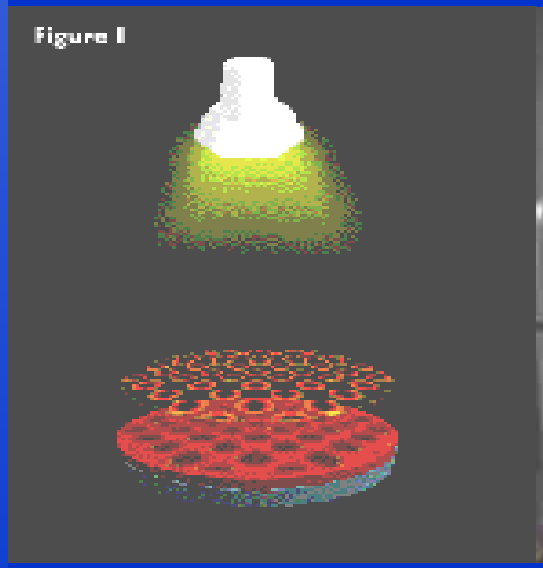
Development of concept to fabricate **separation nozzles** for uranium enrichment at IKVT/KfK (today IMT/FZK)

Many thousands of nozzles cascaded in an array



LiGA Process

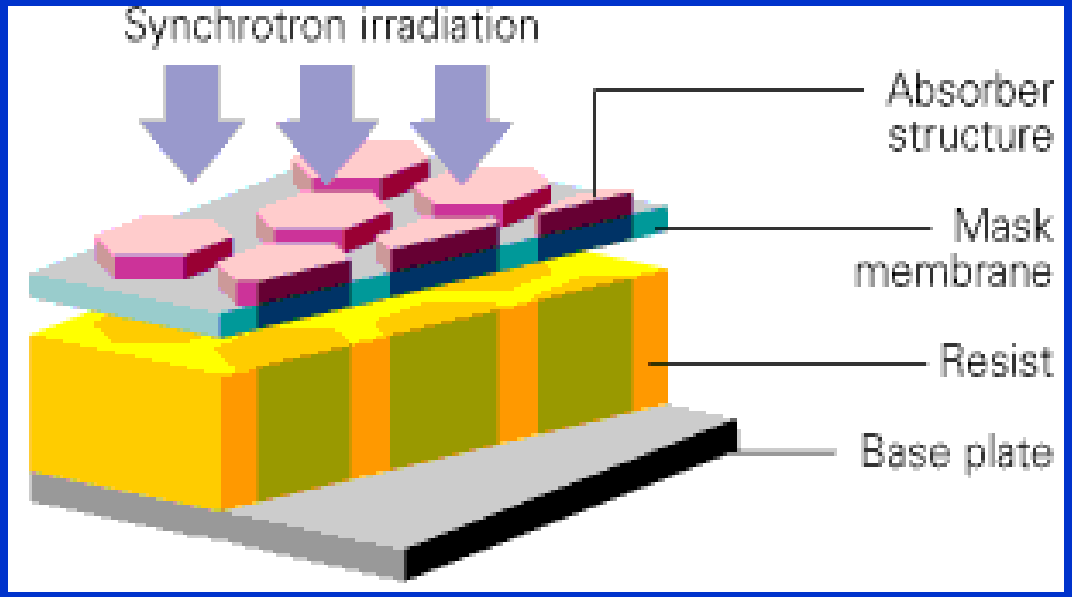
- L i :Lithography
- G : Electroforming
- A : Molding

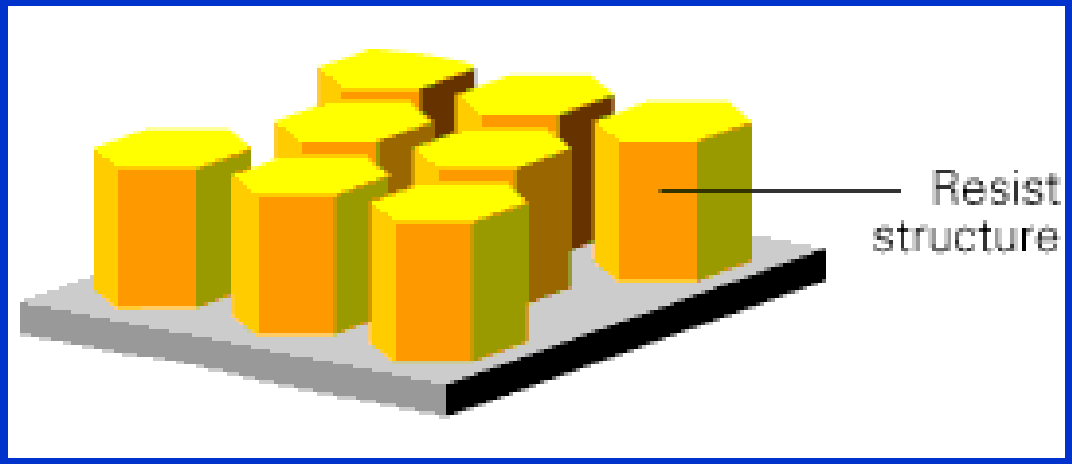


Microfabrication

1. Idea / Project
2. Drawing
3. Optical Masks
4. X-Ray Masks
5. Substrate preparation
6. Exposure
7. Development
8. Electroplating
9. Mold insert final work
10. Device replication
11. Testing
12. Results / Analysis

Lithography





Shadow printing using x-rays

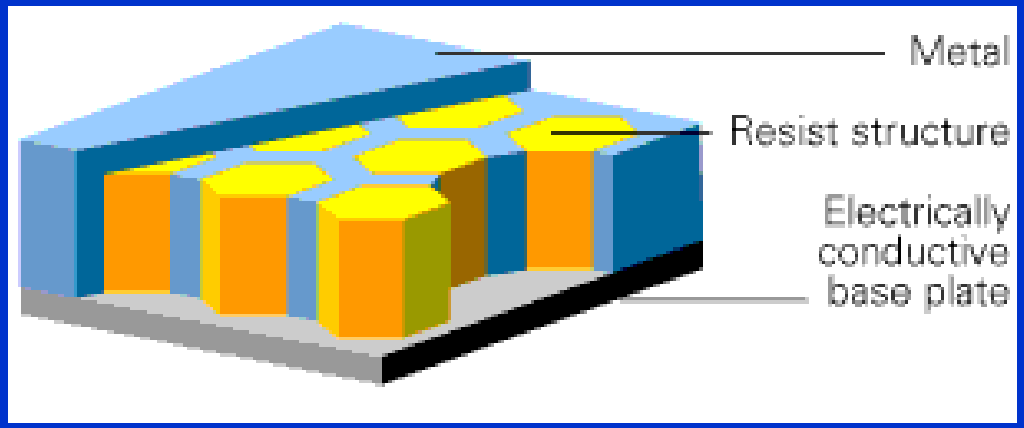
X-ray mask

Resist

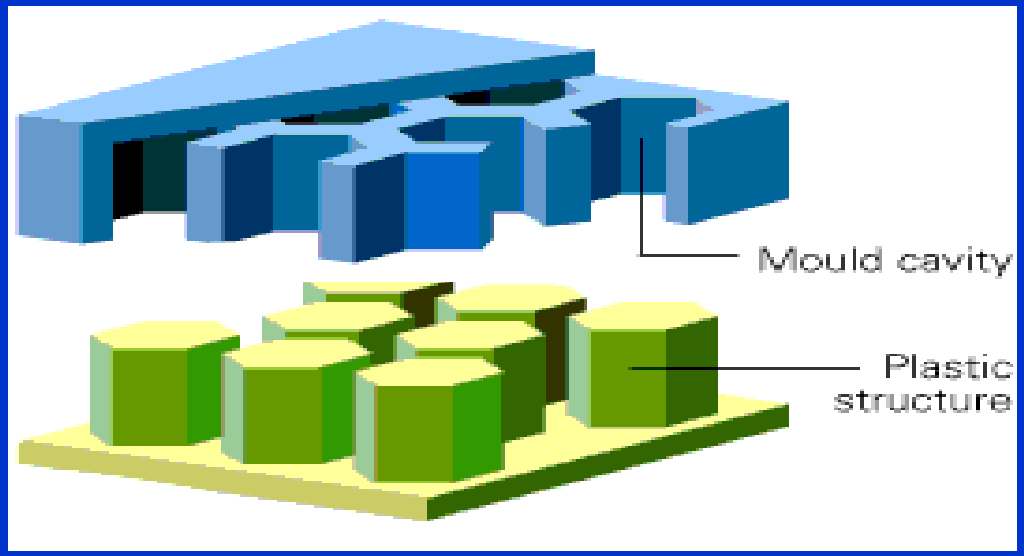
Substrate

Development

Electroforming and Molding

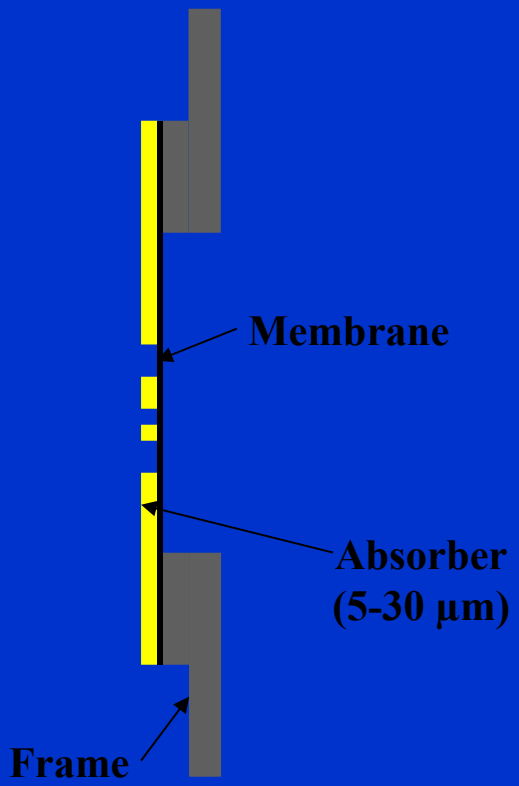


Electroplating of metal structures and mold inserts



Replication by molding (hot embossing, injection molding)

X-ray masks



Desirable mask membrane characteristics

- Good X-ray and optical transmission
- Good mechanical stability, low internal stress
- Radiation resistant
- Compatible with established mask making processes and equipment
- Compatible with plating of Au absorber

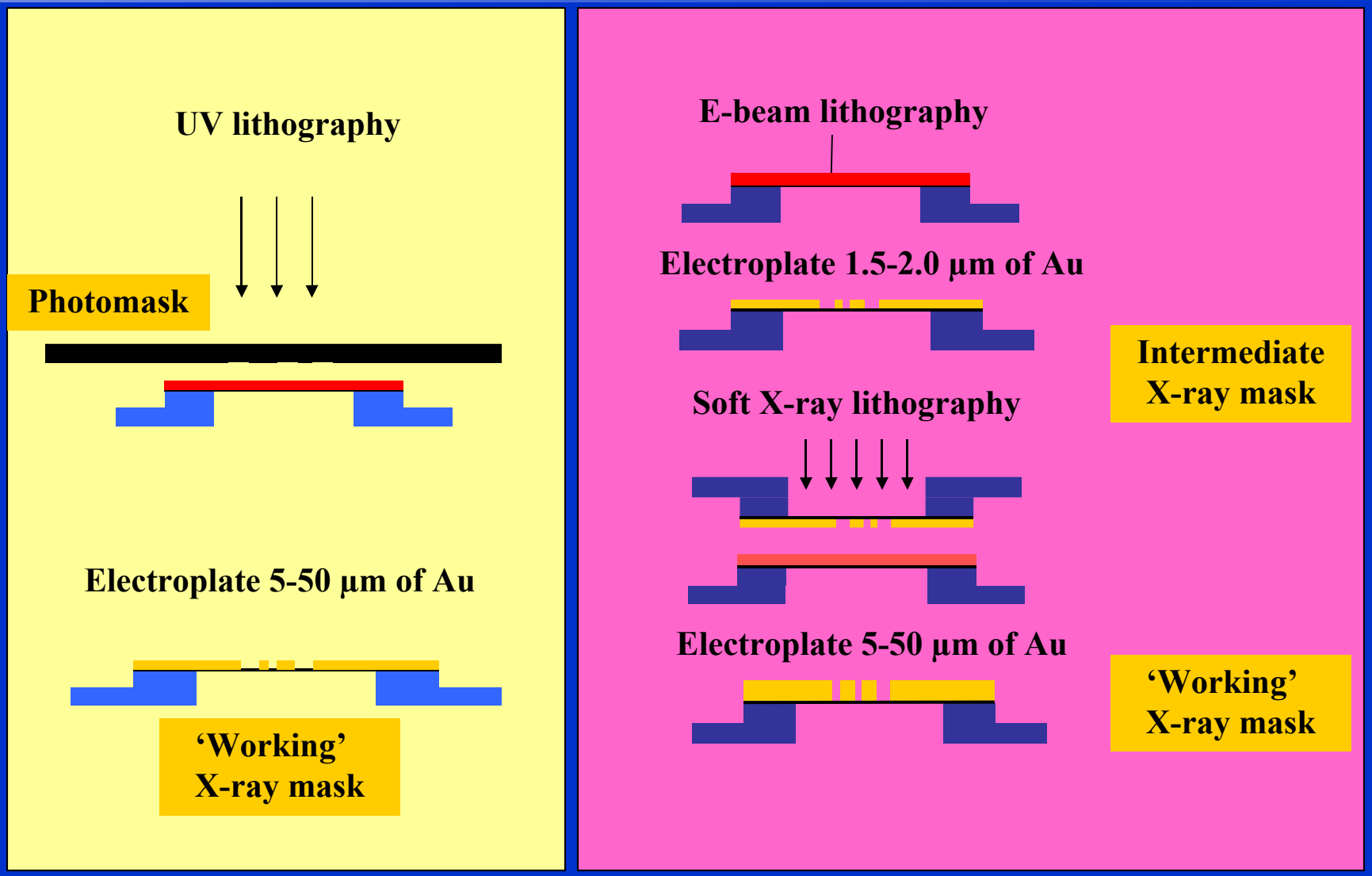
Thin membranes:

Silicon, Silicon Nitride, Titanium, Diamond

Thick low Z substrates:

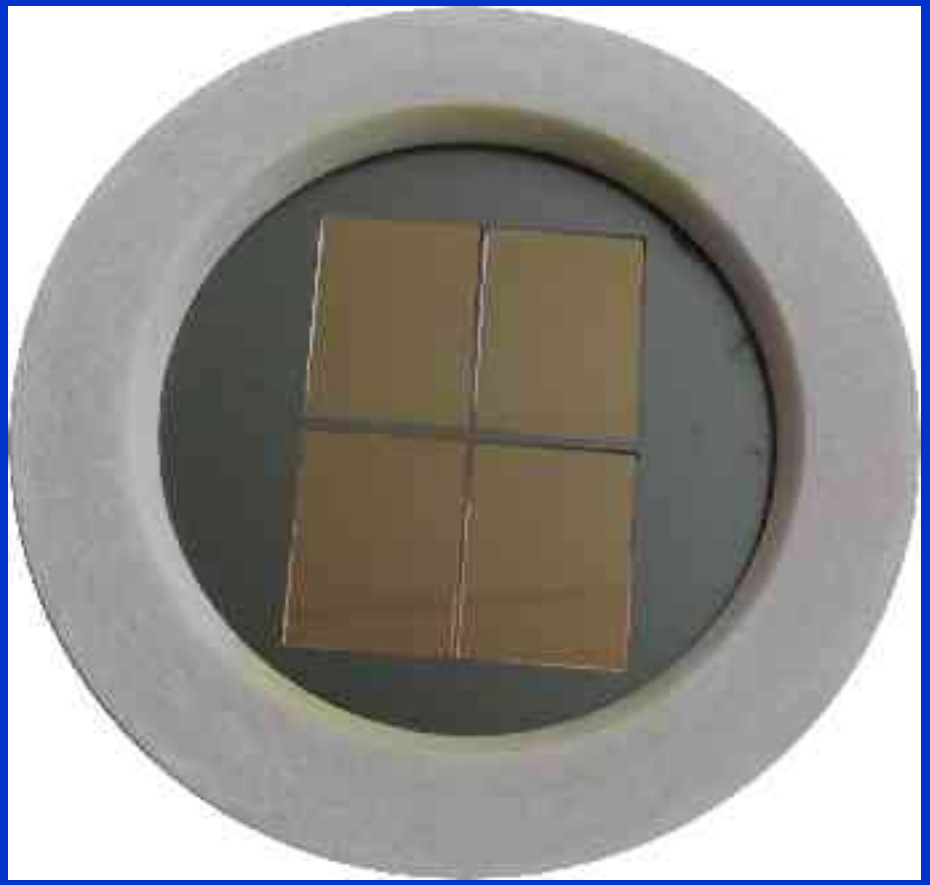
Graphite, Beryllium, Silicon, glass

Mask fabrication



Thin membrane

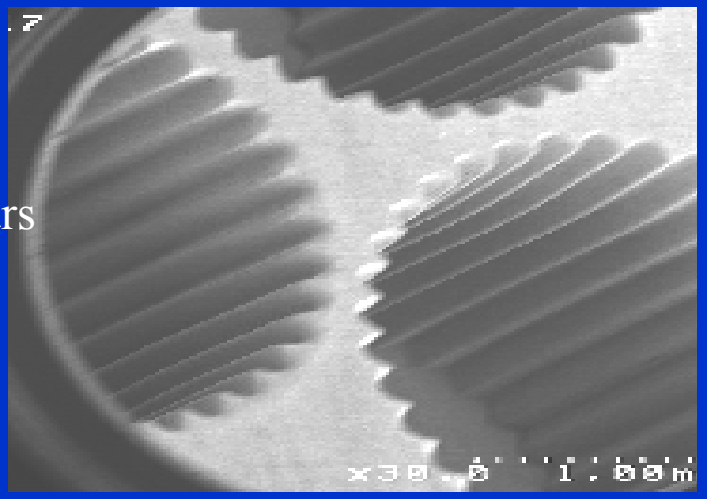
Silicon etching setup for making 1 μm thick Silicon Nitride Membrane



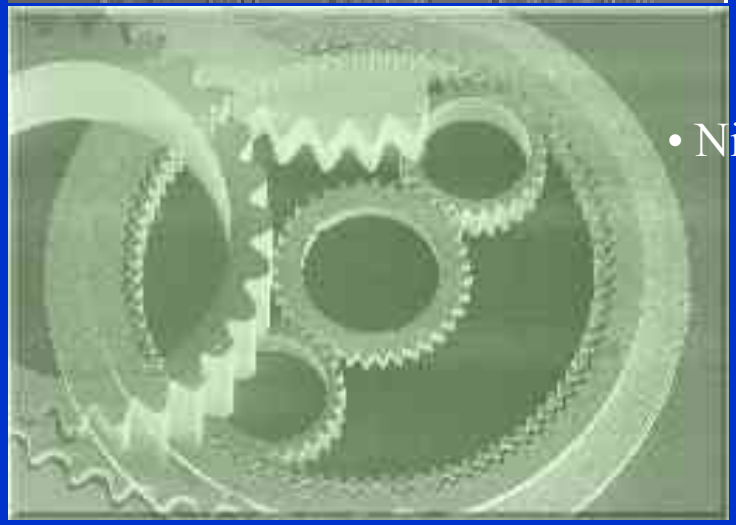
Window size 4×20×33mm

Properties of …

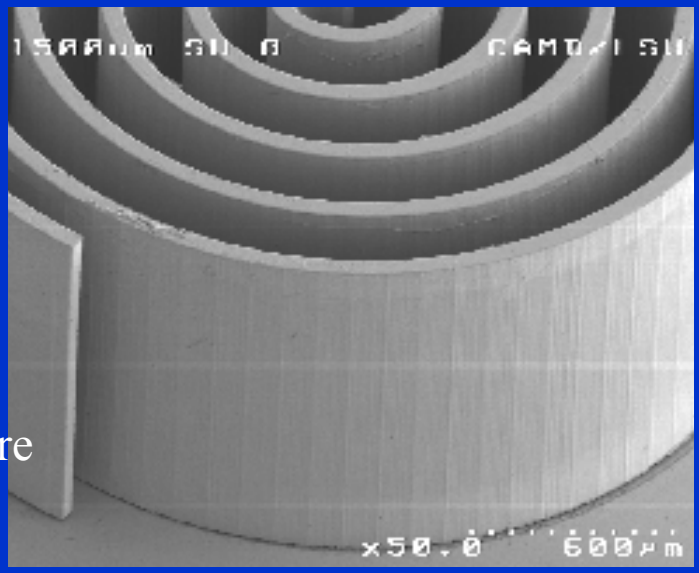
•2500 µm tall templates for micro-gears



•Sub-micrometer structural details



• NiFe gear assembly

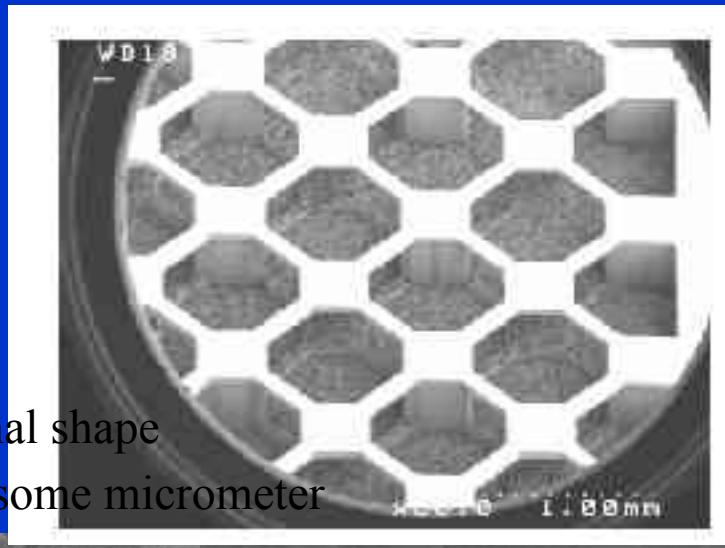


•Extreme structure heights

… LiGA Microstructures

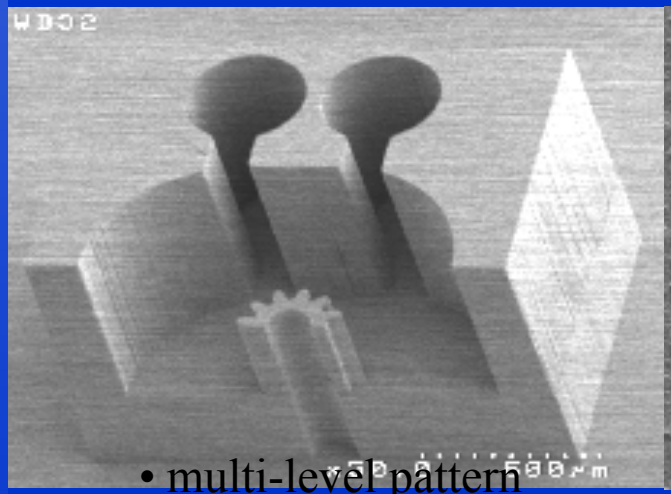
• non-vertical sidewalls

• **Wide variety of materials possible**

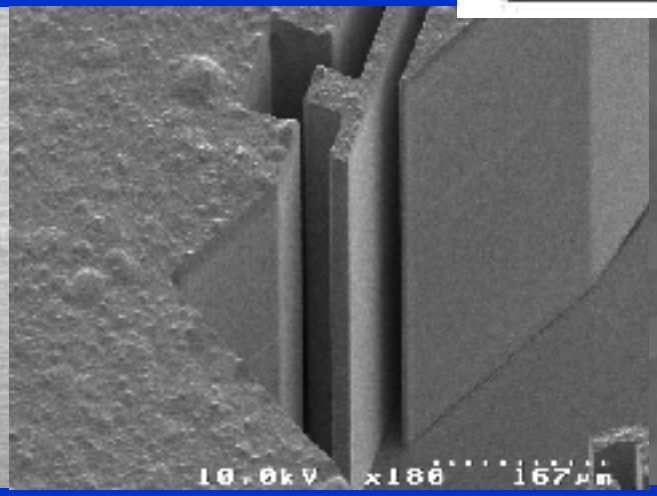


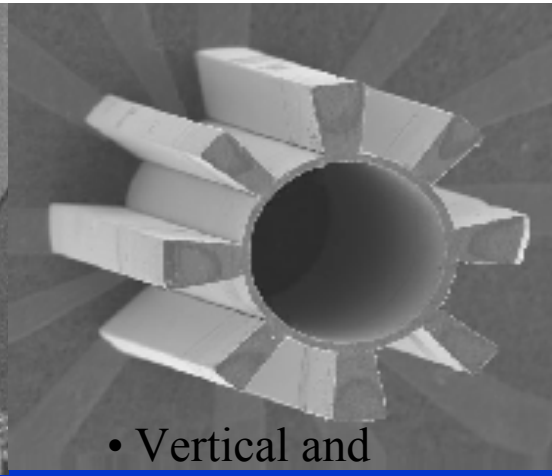
•Arbitrary cross-sectional shape

•Smallest structures of some micrometer



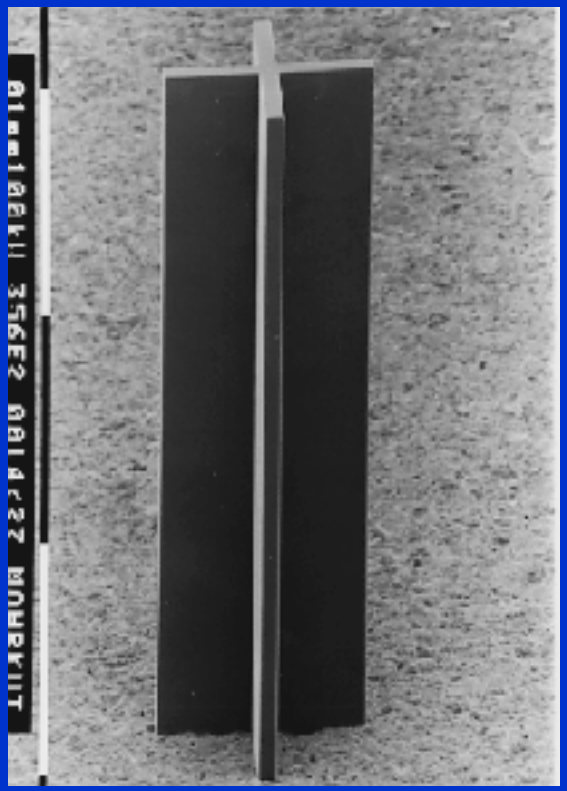
• multi-level pattern

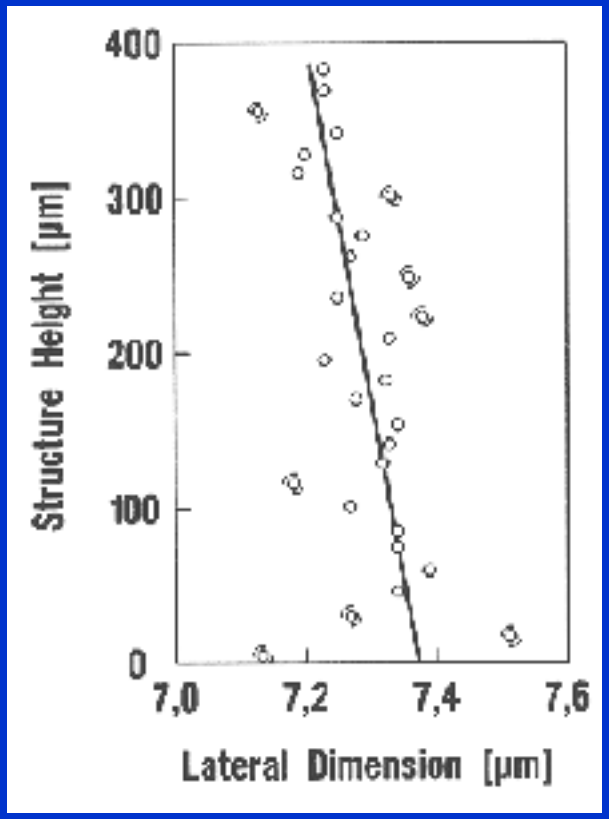




• Vertical and smooth sidewall

Patterning Accuracy - DXRL





Deviation from perfect sidewall ~ 0.06µm / 100 µm

Ph.D. Thesis Jürgen Mohr, IMT/FZK, 1987

Mold insert

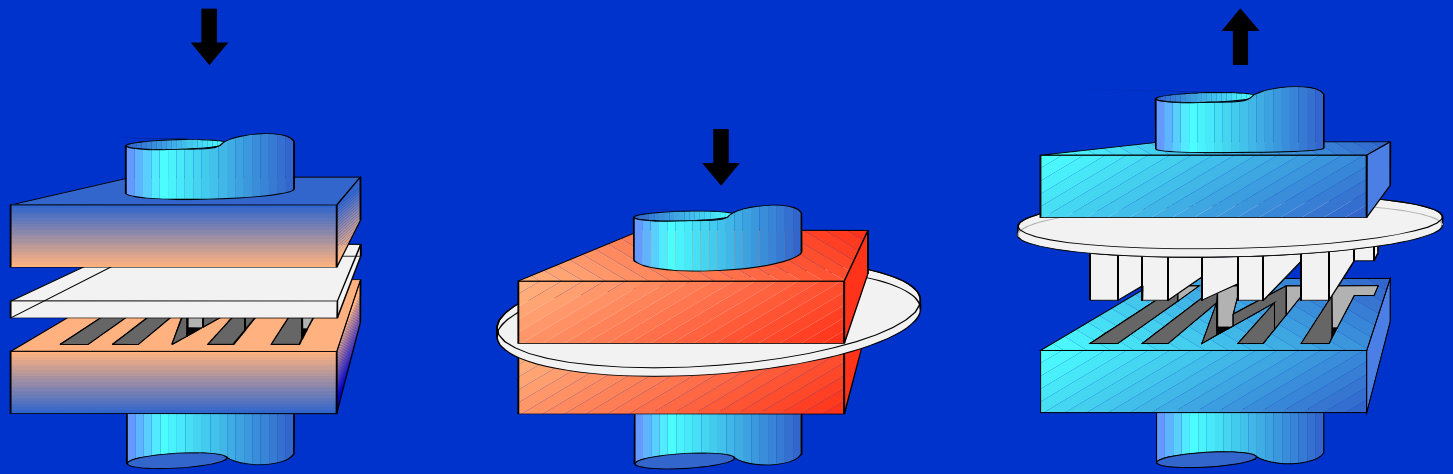
Overplating

Nickel Mold insert

Hot embossing

- **A thermo-plastic replication process suitable for LiGA HARM structures.**
- **Key process steps include heating, evacuating, stamping, and demolding.**

Replication process



Insert plastic, close press, evacuate, and heat up.

Apply high pressure to transfer structures.

Cool down, vent, and demold structured plastic parts.

LiGA Process

Definition

To make things clear….

XRL or soft XRL:	**X-ray lithography in thin resists**
DXRL:	**Deep X-ray lithography (up to 1mm)**
UDXRL:	**Ultra-deep x-ray lithography (above 1mm)**

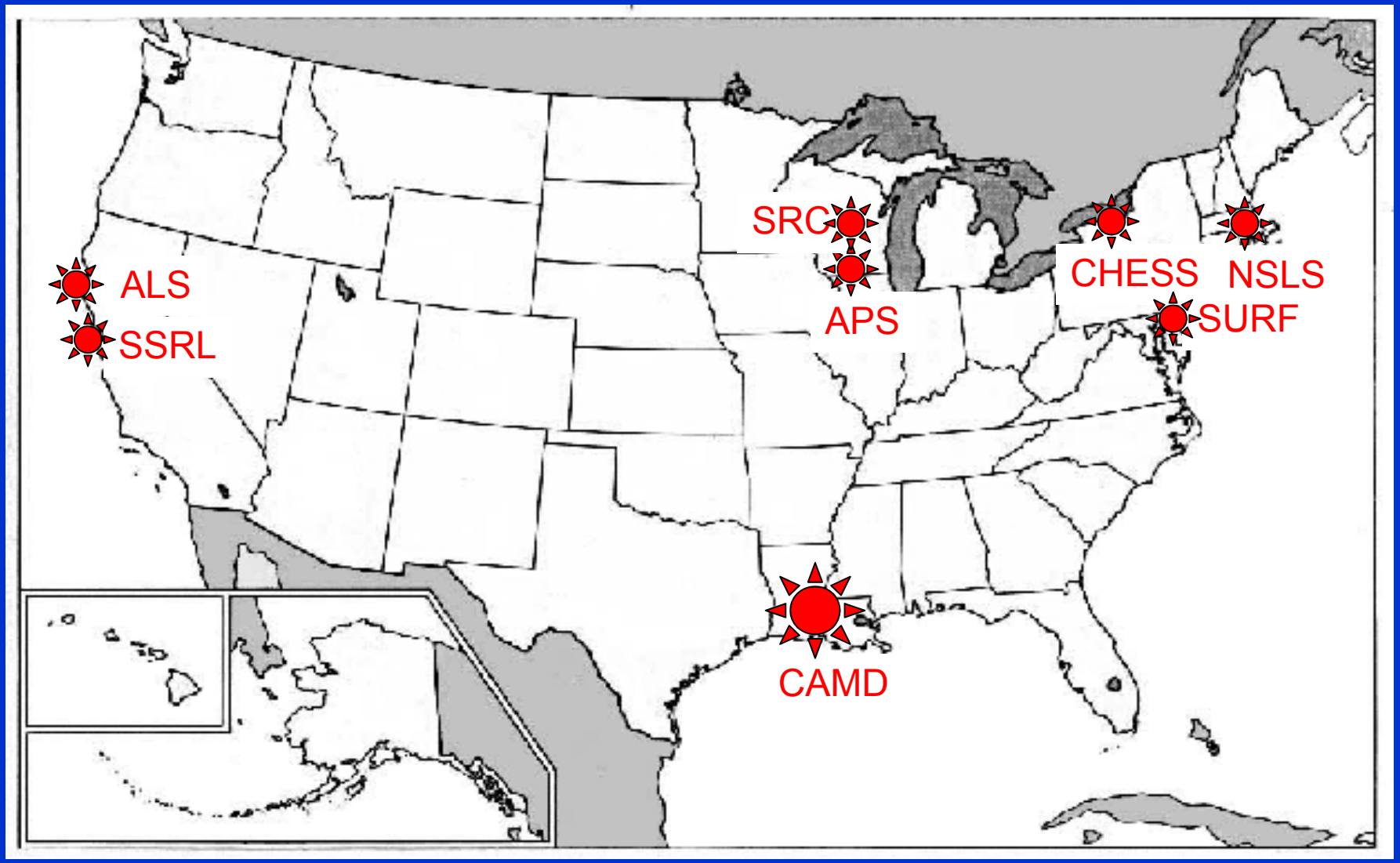
LiGA is not to make the next generation micro-chips.

It is a ultra-precision micromachining process using lithographic tools !

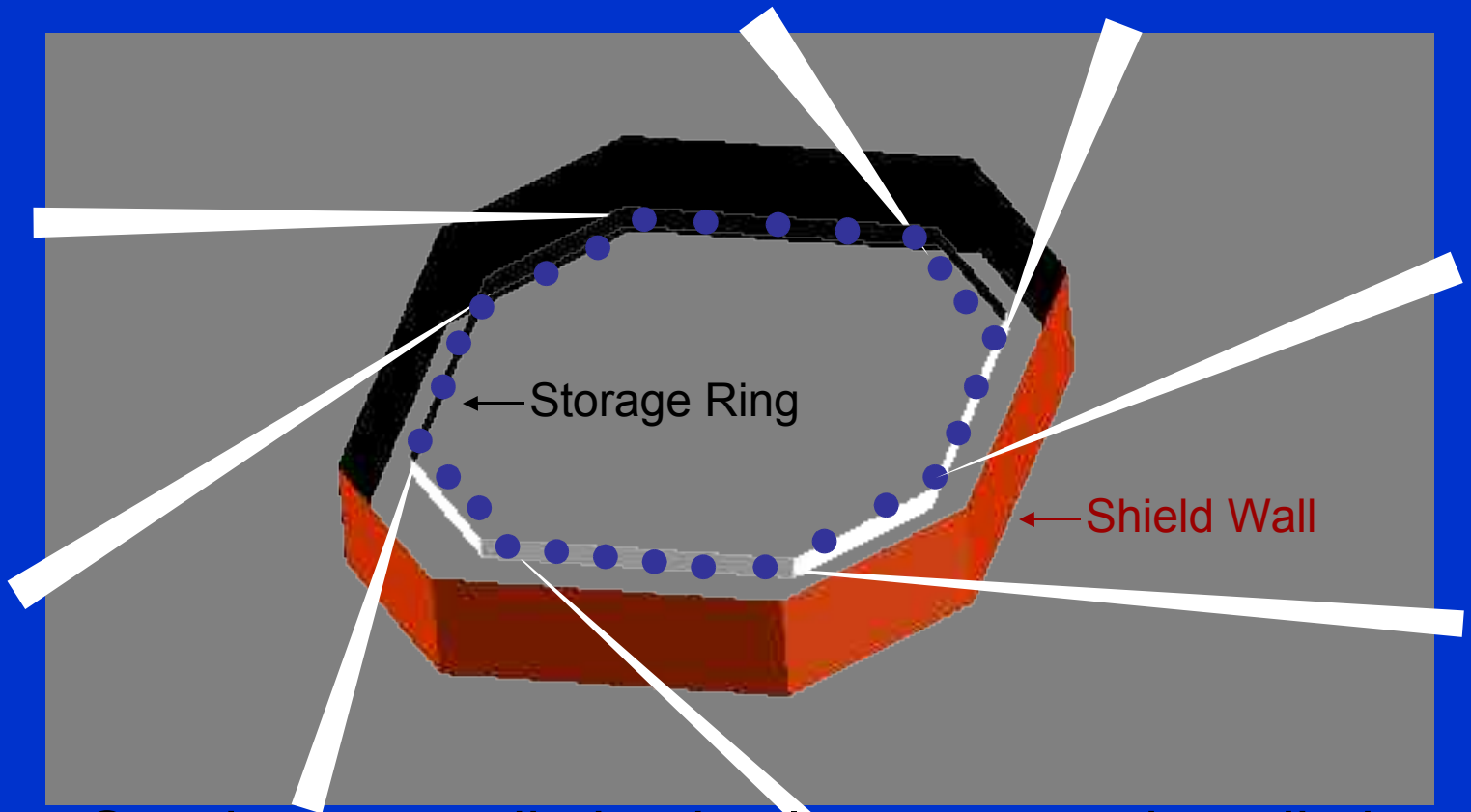
CAMD – LSU

a Synchrotron Radiation Facility Dedicated to Microfabrication

Synchrotrons in the U.S.



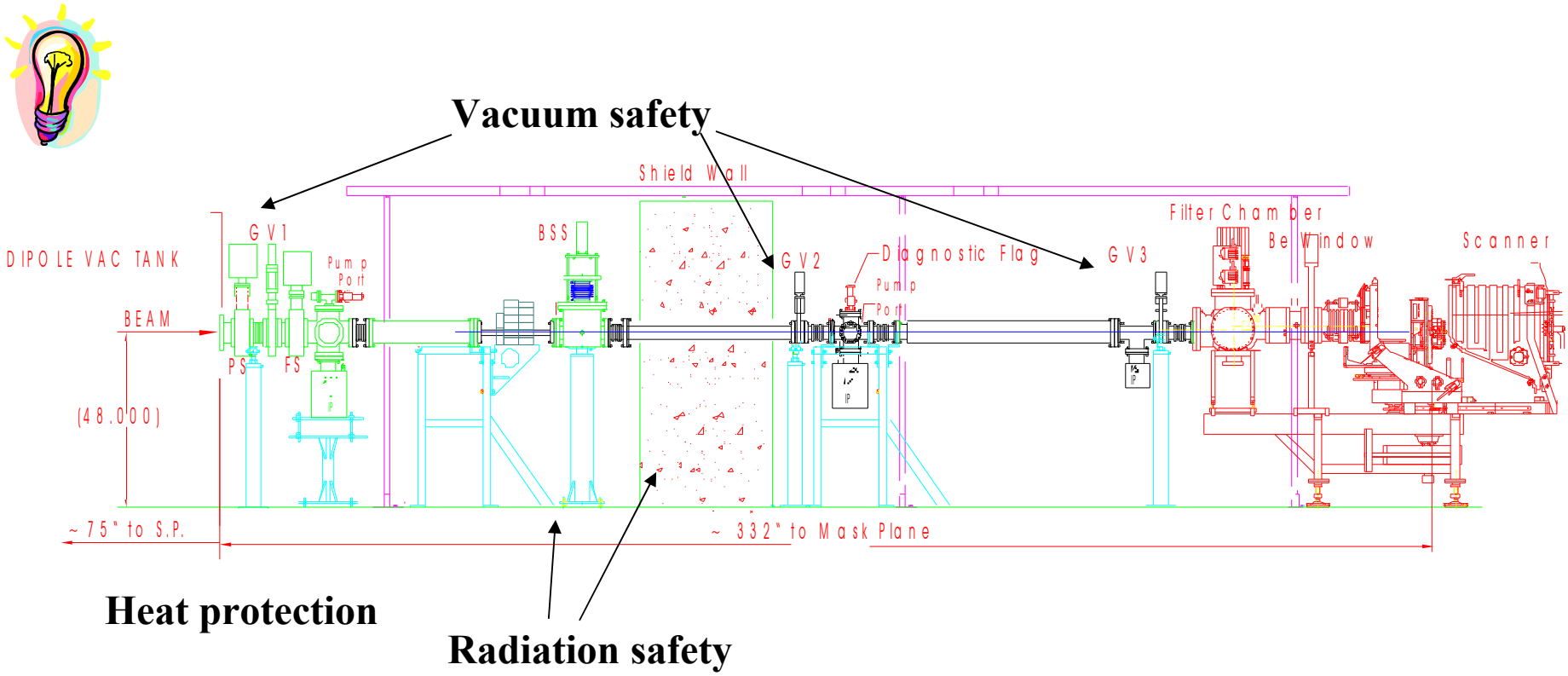
Synchrotron Radiation



Synchrotron radiation is electromagnetic radiation (light) emitted from electrons (positrons) moving with relativistic velocities on macroscopic circular orbits.

Lightening the sample

- 4 Synchrotron lines operating at 1.3 - 1.5 GeV for μfab
- 1 for SOFT X-rays from Cr double mirror system
- 1 for HARD X-rays from 7 T Wiggler



Some Infrastructure at CAMD

Oxford ion milling

Inside the clean room

Quintel
UV aligner

Temescal e-beam
evaporator

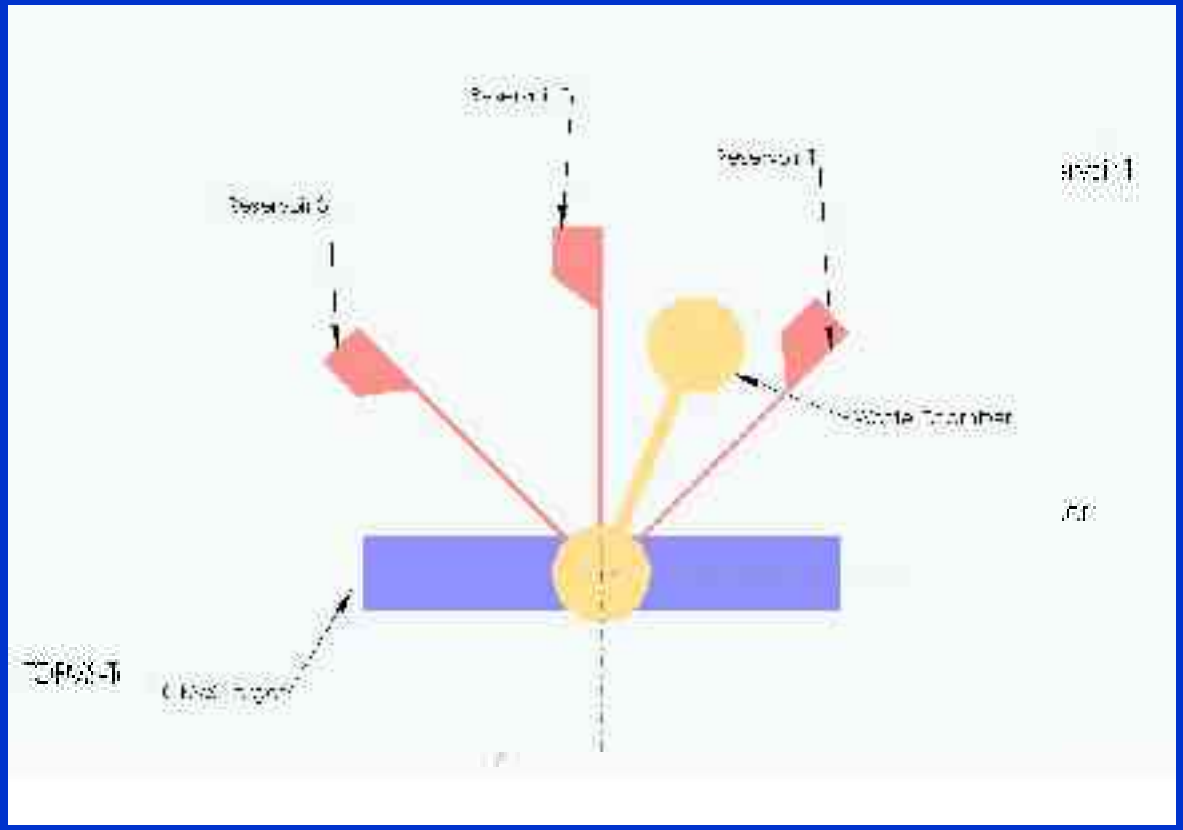
Plating Station

and more …

CAMD Infrastructure

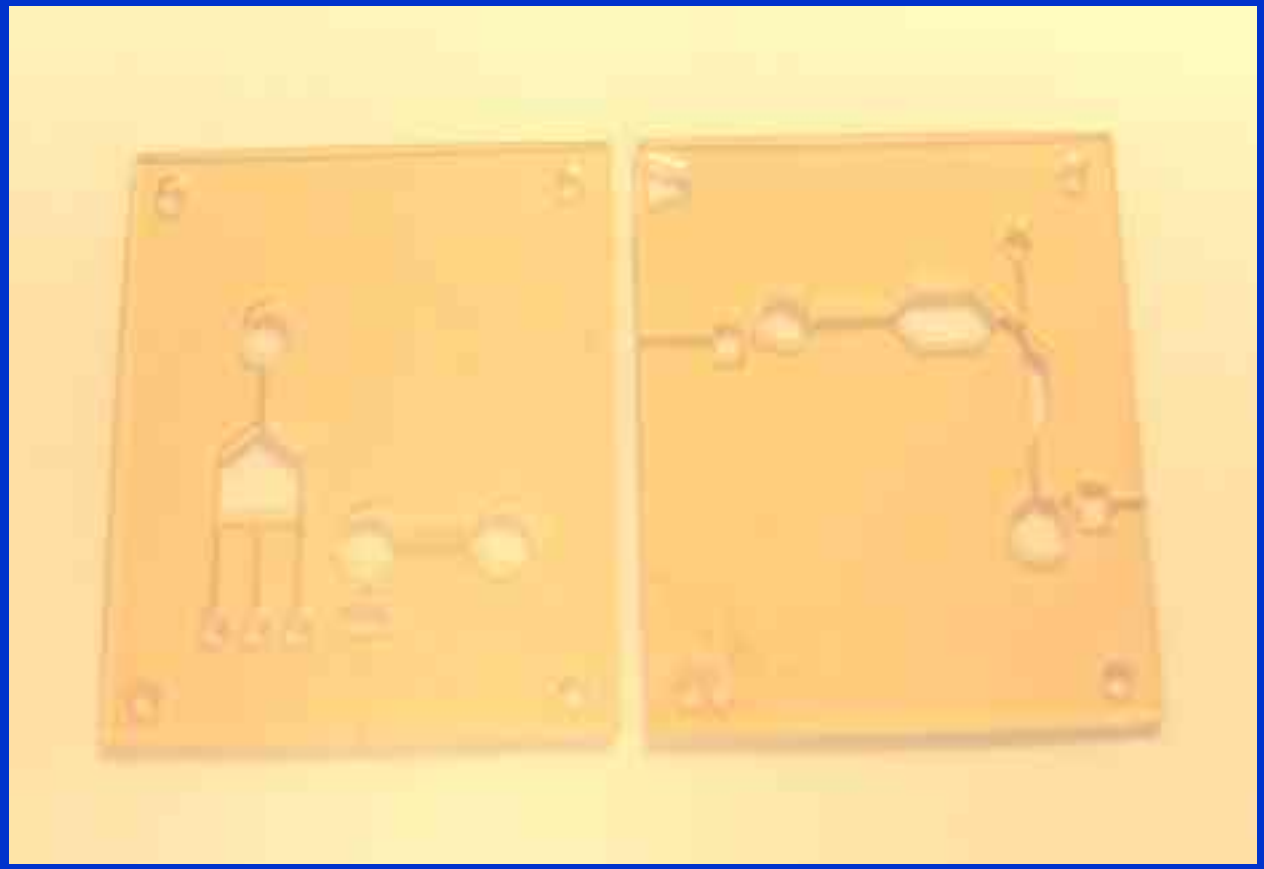
- **Metrology**
- **Material characterization**
- **Chemistry lab**
- **Surface finishing**
- **Molding**

Concept of 3D μ–Fluidic-S

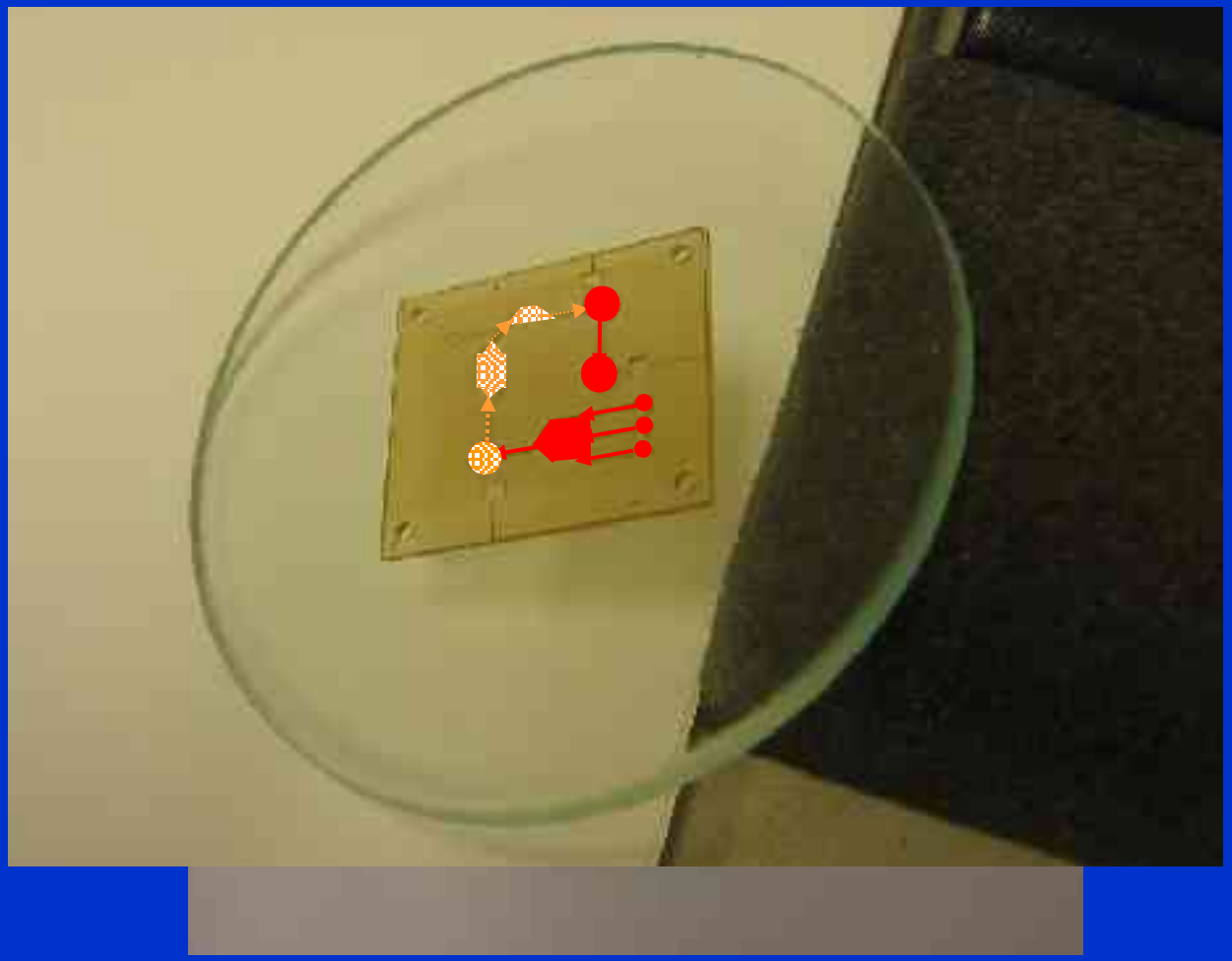


Modular Test Structure

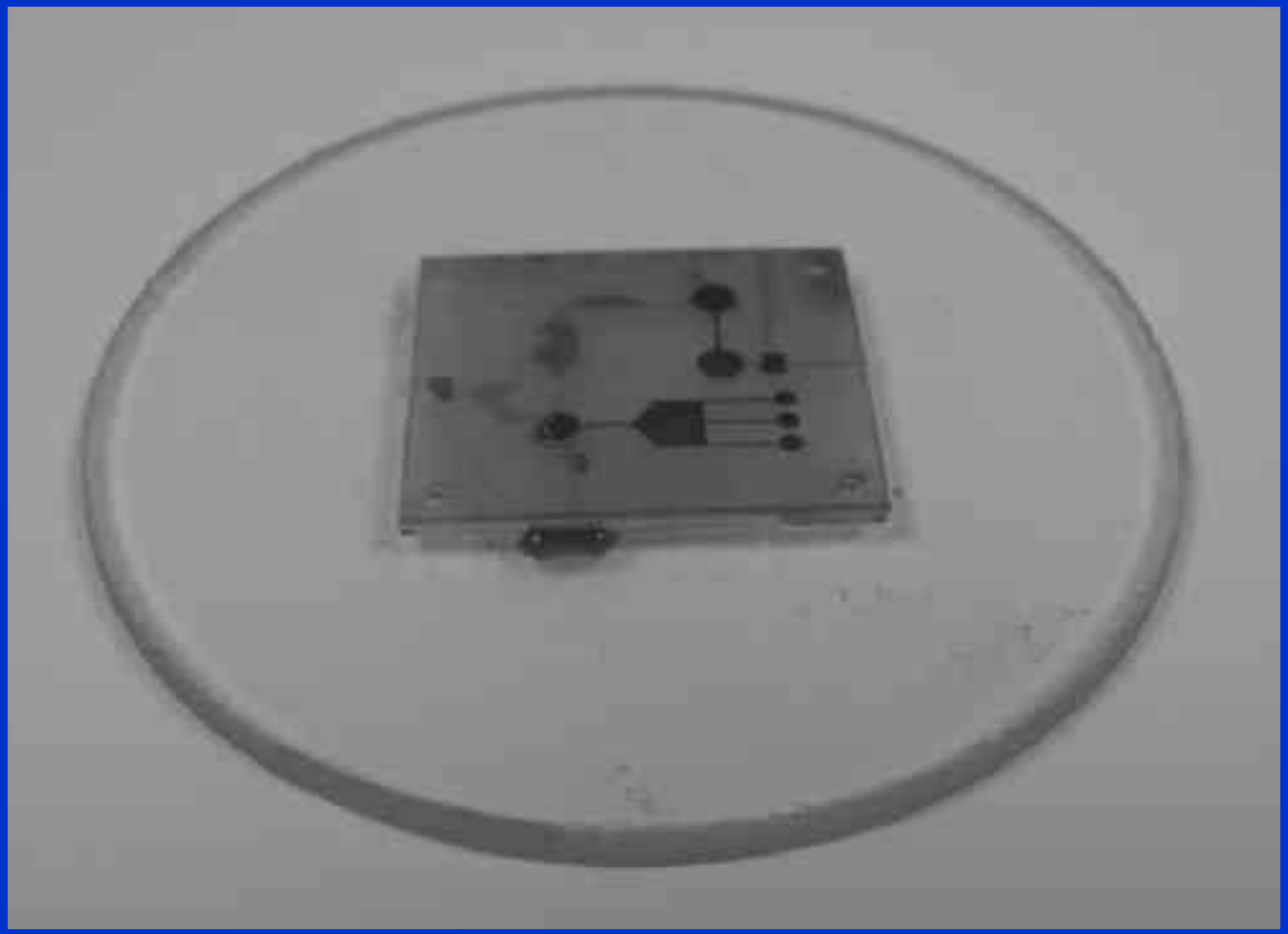
- Molded Modular Micro-fluidic Structure



Multilevel Microfluidic Device

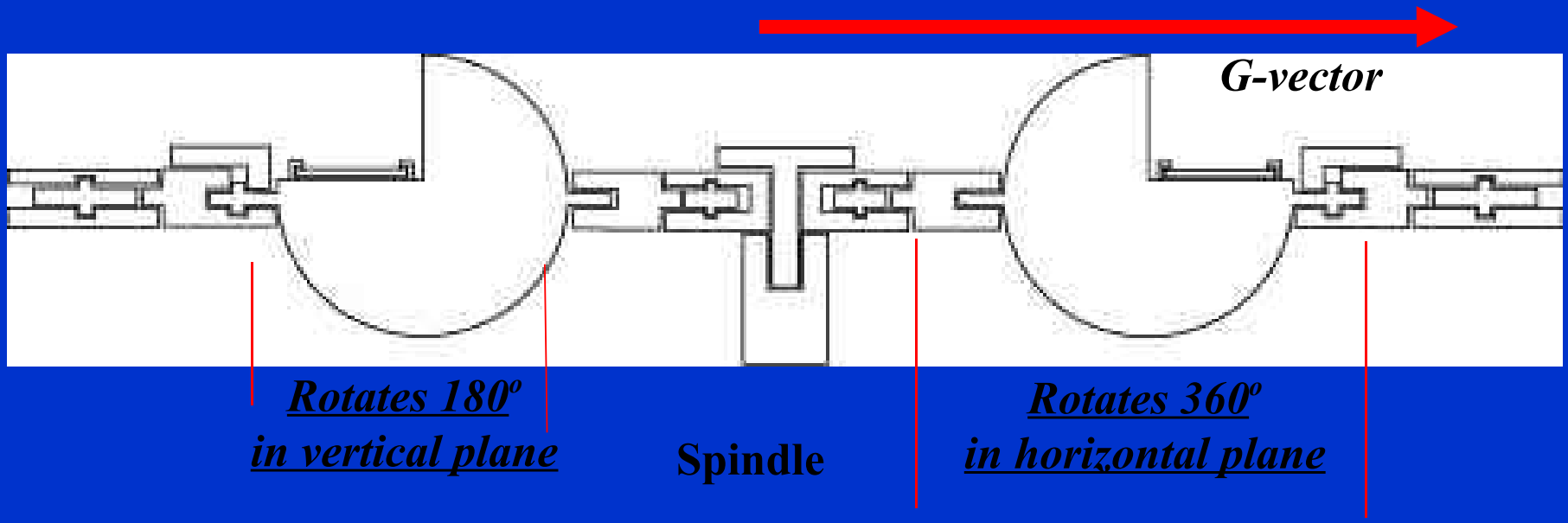


Result



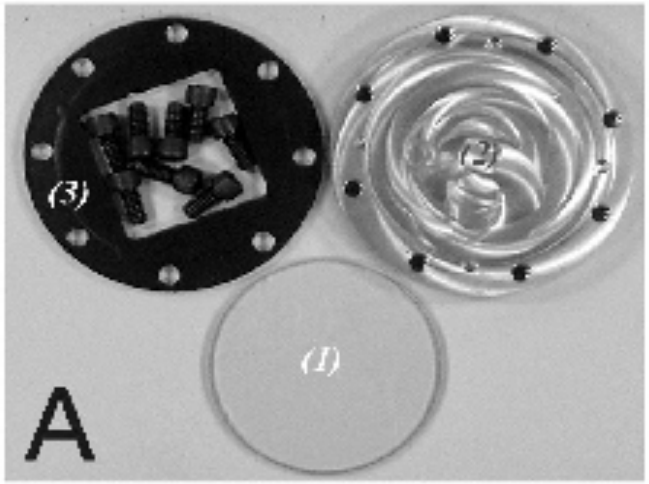
Lab-on-a-CD – Centrifugal Bio-Chips For the Analysis of Biologically Fluid Samples

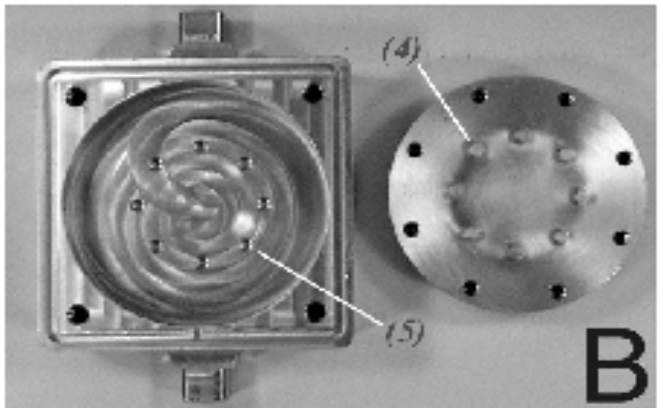
Centrifugal Bio-Chips For the Analysis of Biologically Fluid Samples



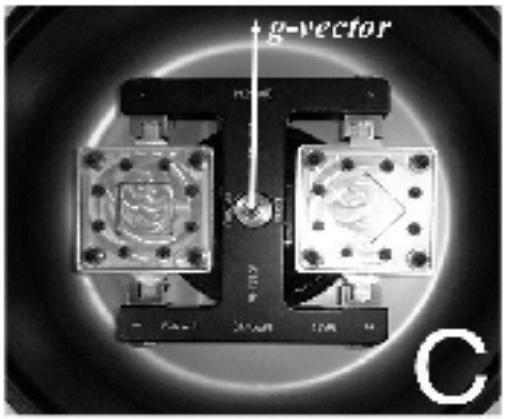
Collaboration: Mark F. Clarke, University of Texas at Houston

Quasi 3D-Centrifuge Micro-Mechanics Parts

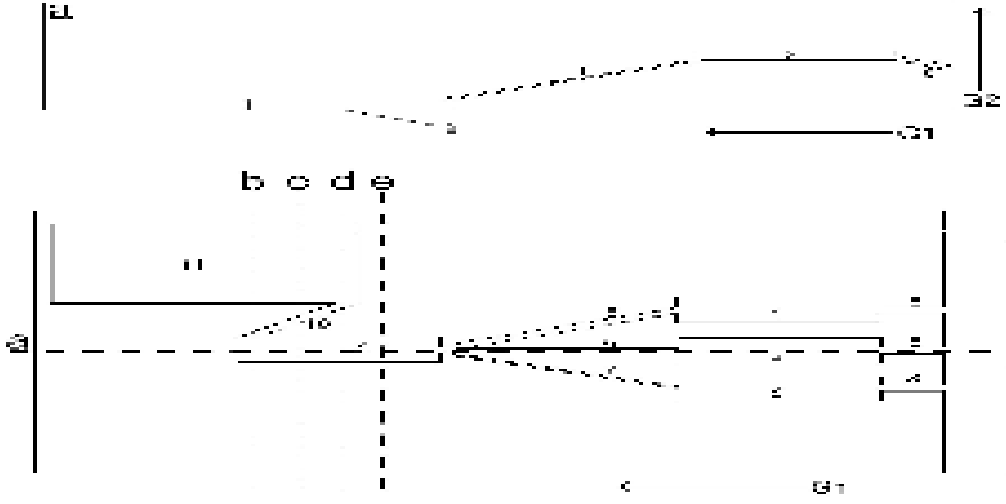




4” or 100mm

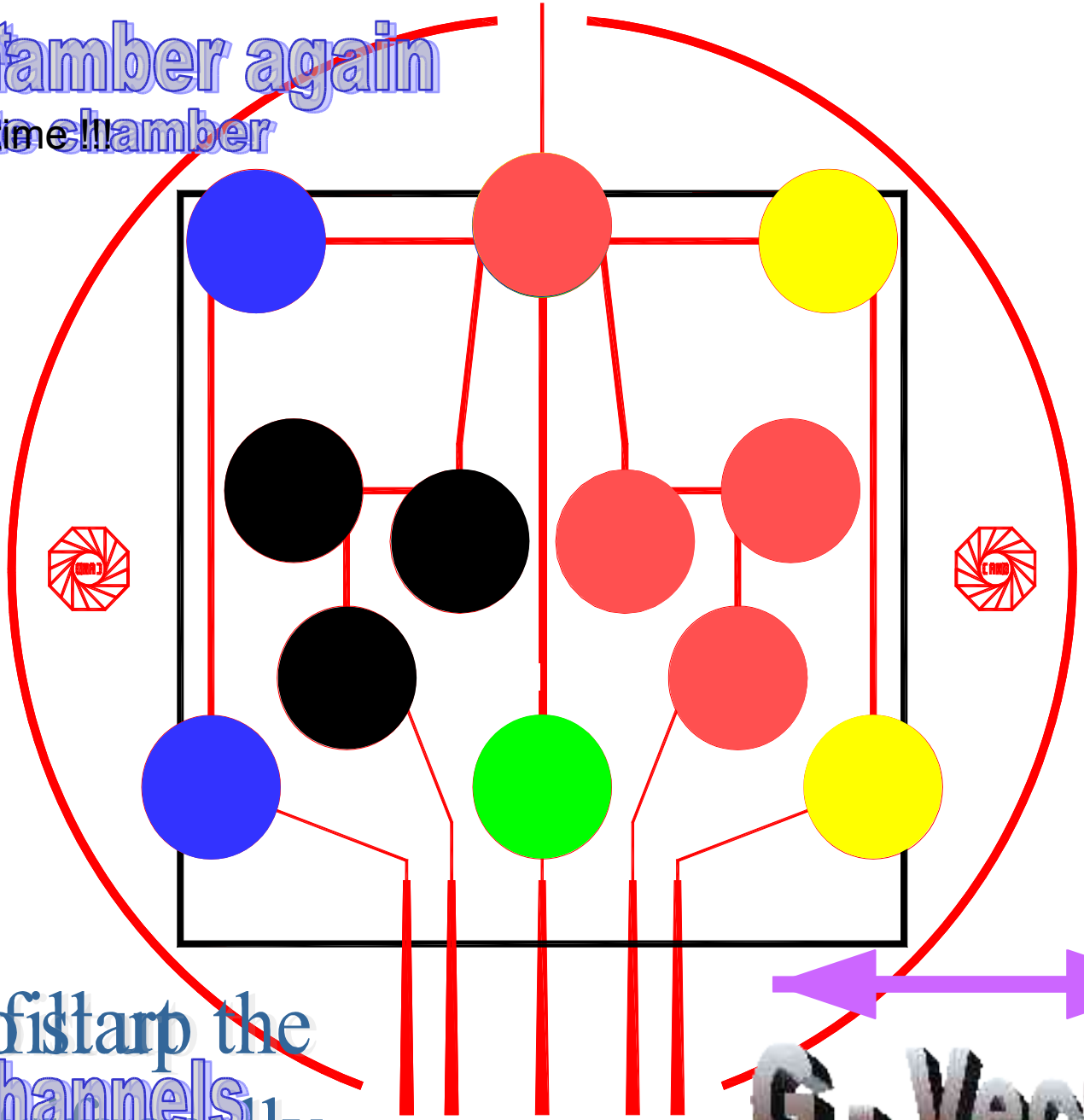


Molded CD



Waste chamber again

Last time !!!



G - Vector

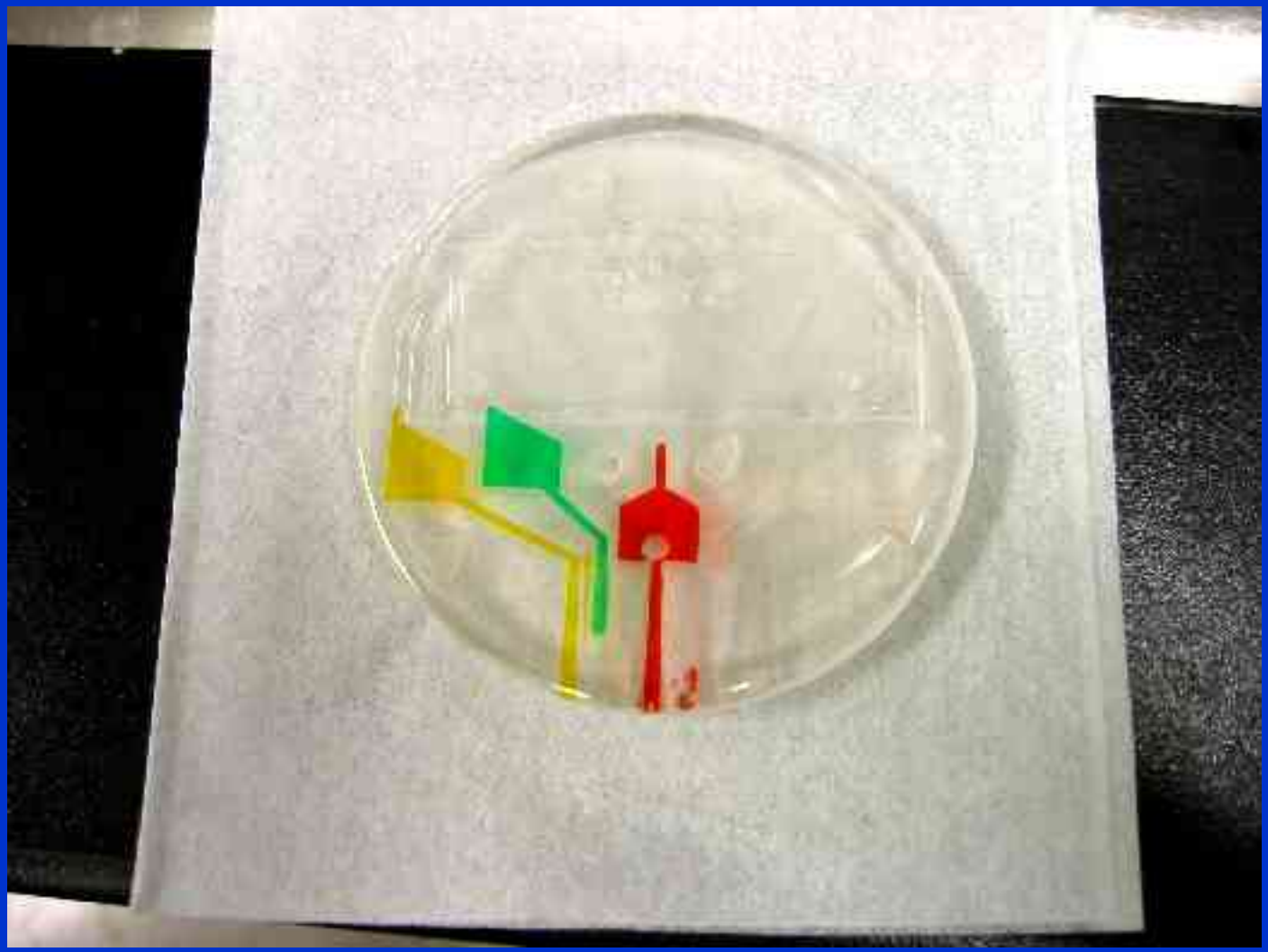
(AGAIN)!!

Fill up the channels

Filling channels

G - Vector

First test

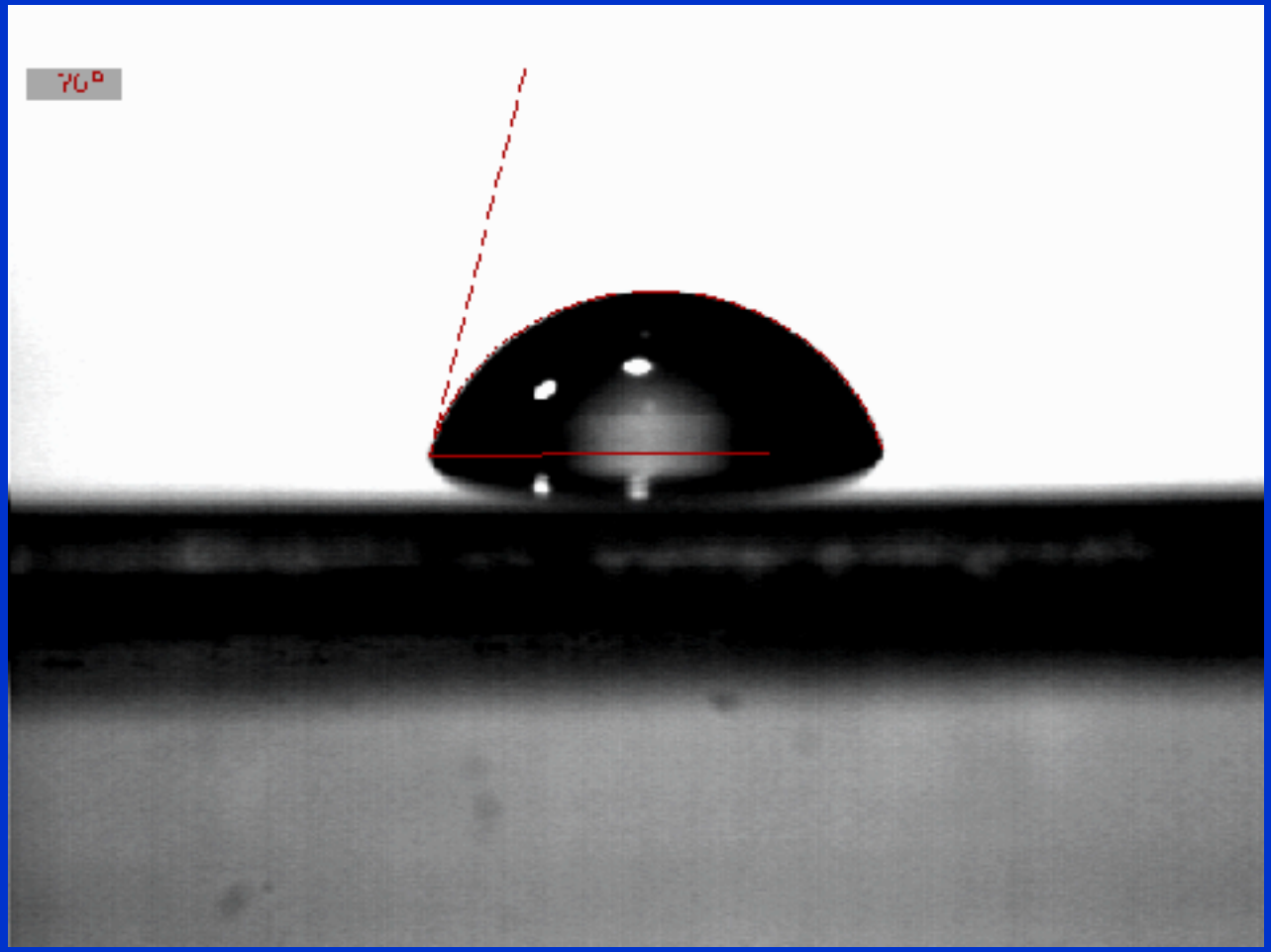


Solutions

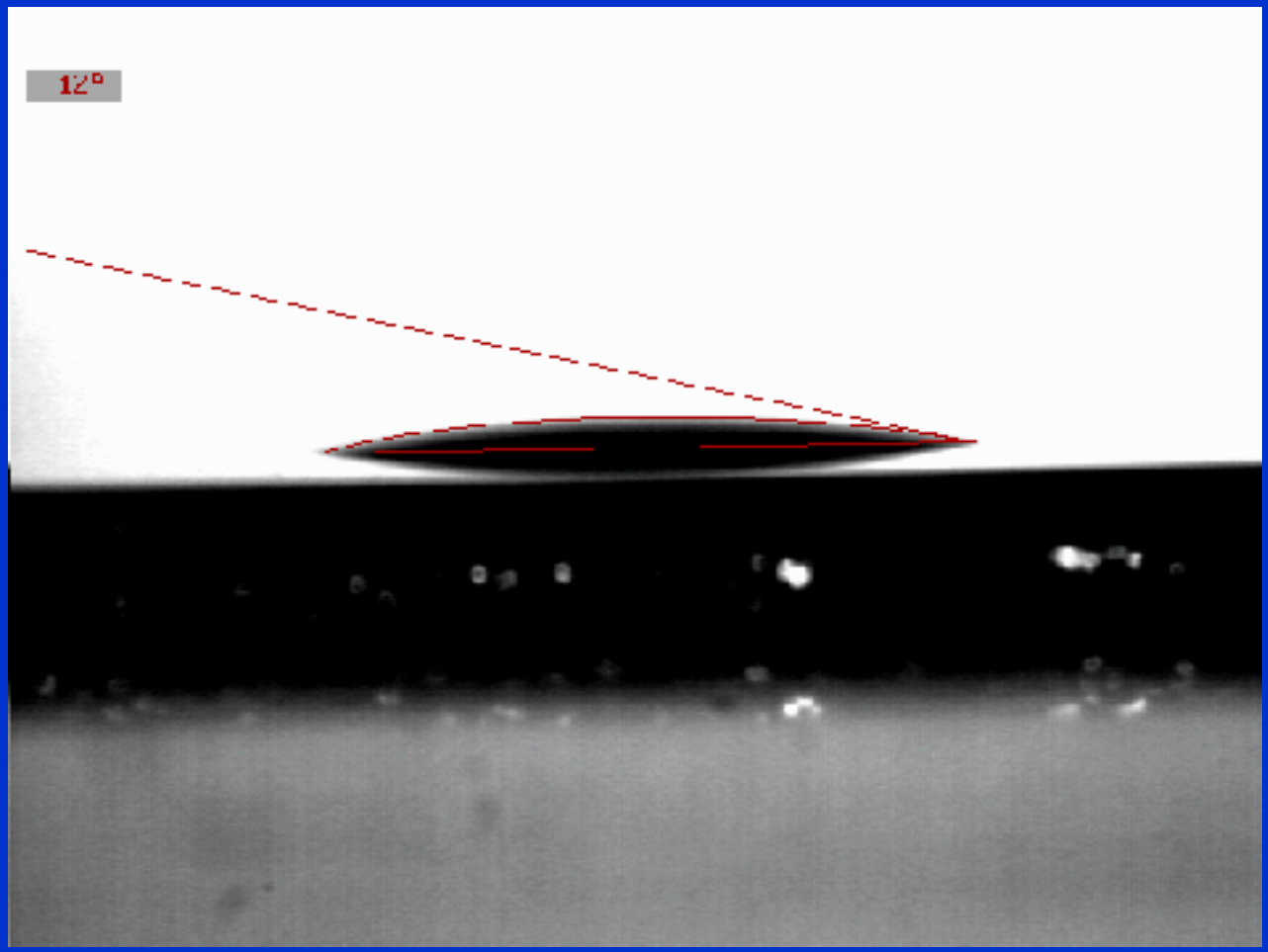
Minimum requirement

- 1) Protein G = IgG immunoglobulins
- 2) Sample containing (or not) Salmonella
- 3) Washing (detergent) solution: rinse

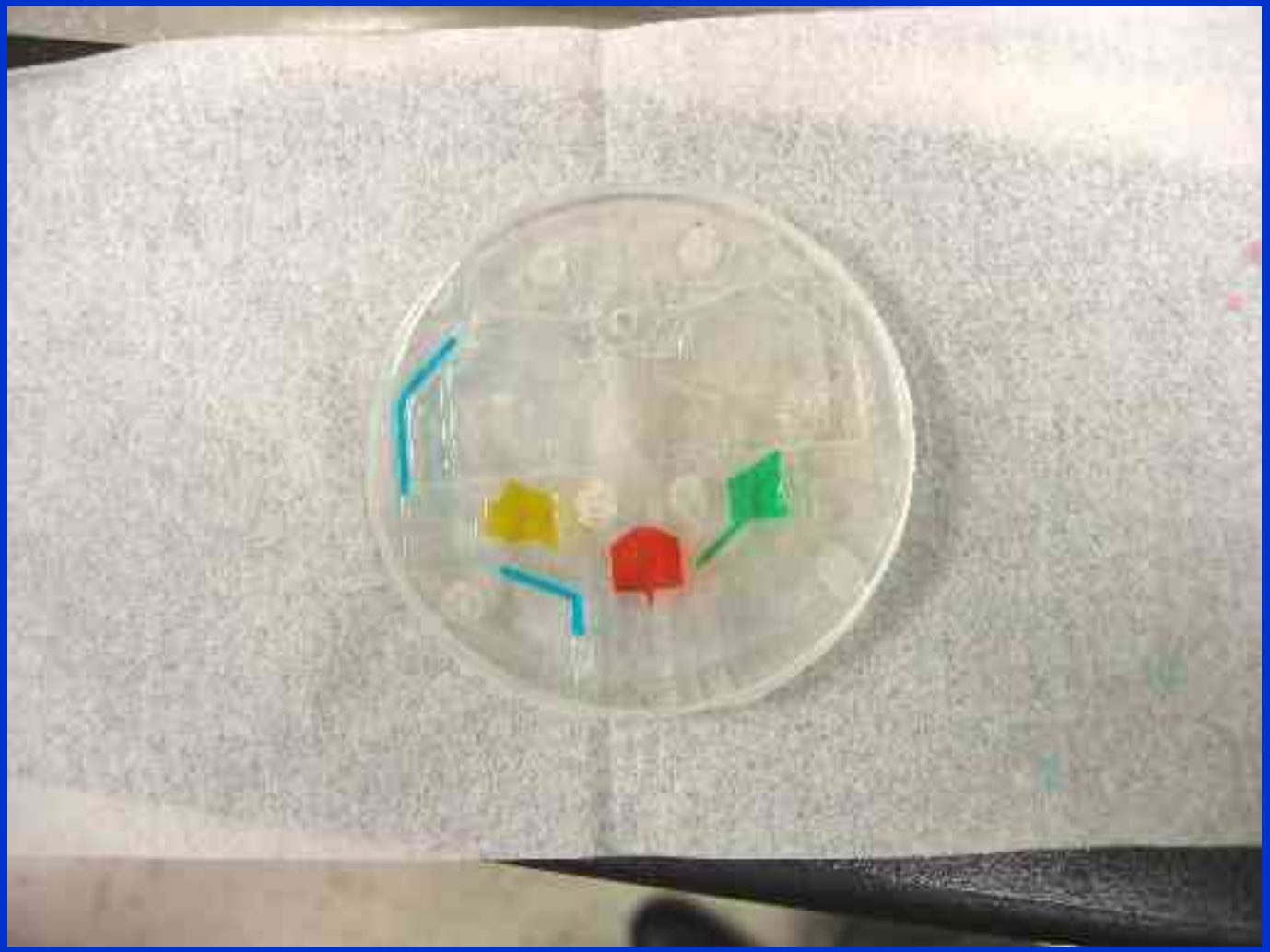
Solution 1 & 2



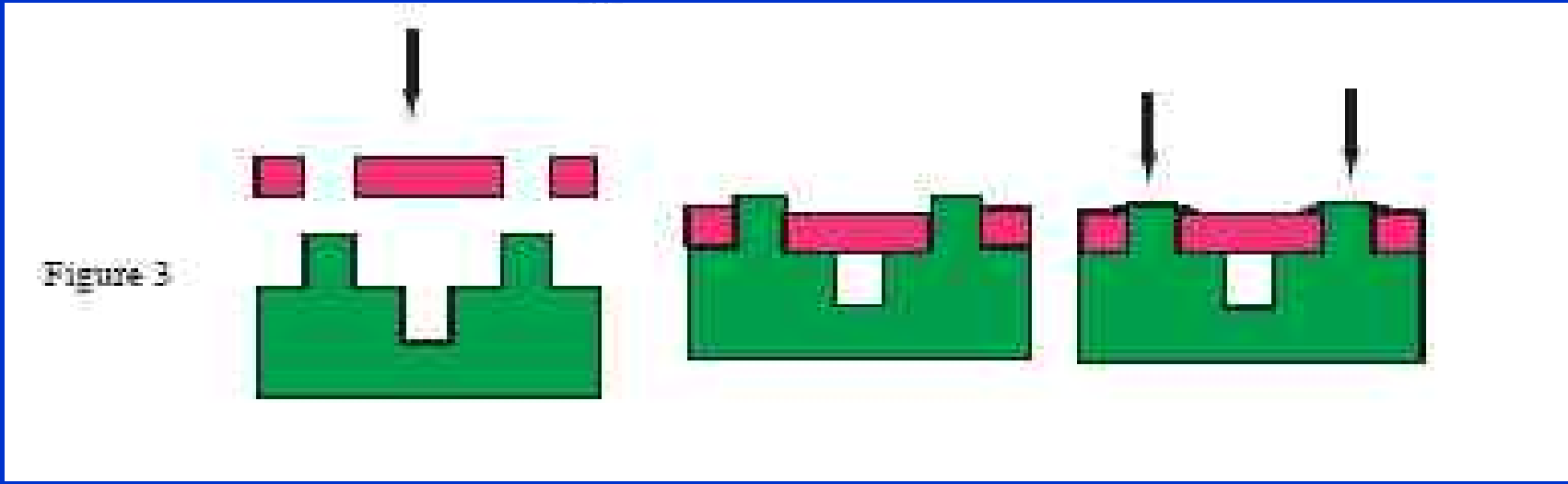
Solution 3



Sealing troubles

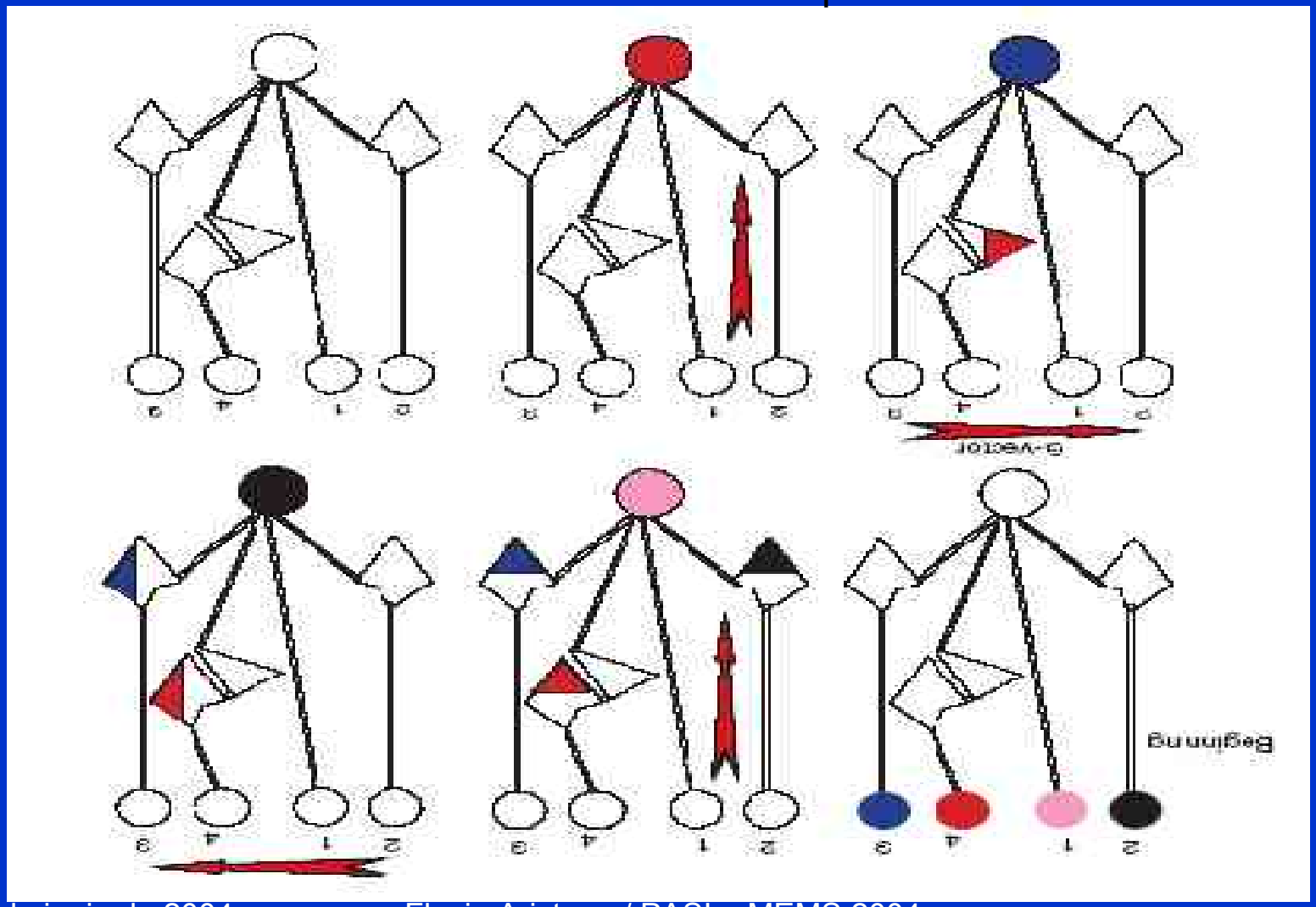


Ideas for Sealing

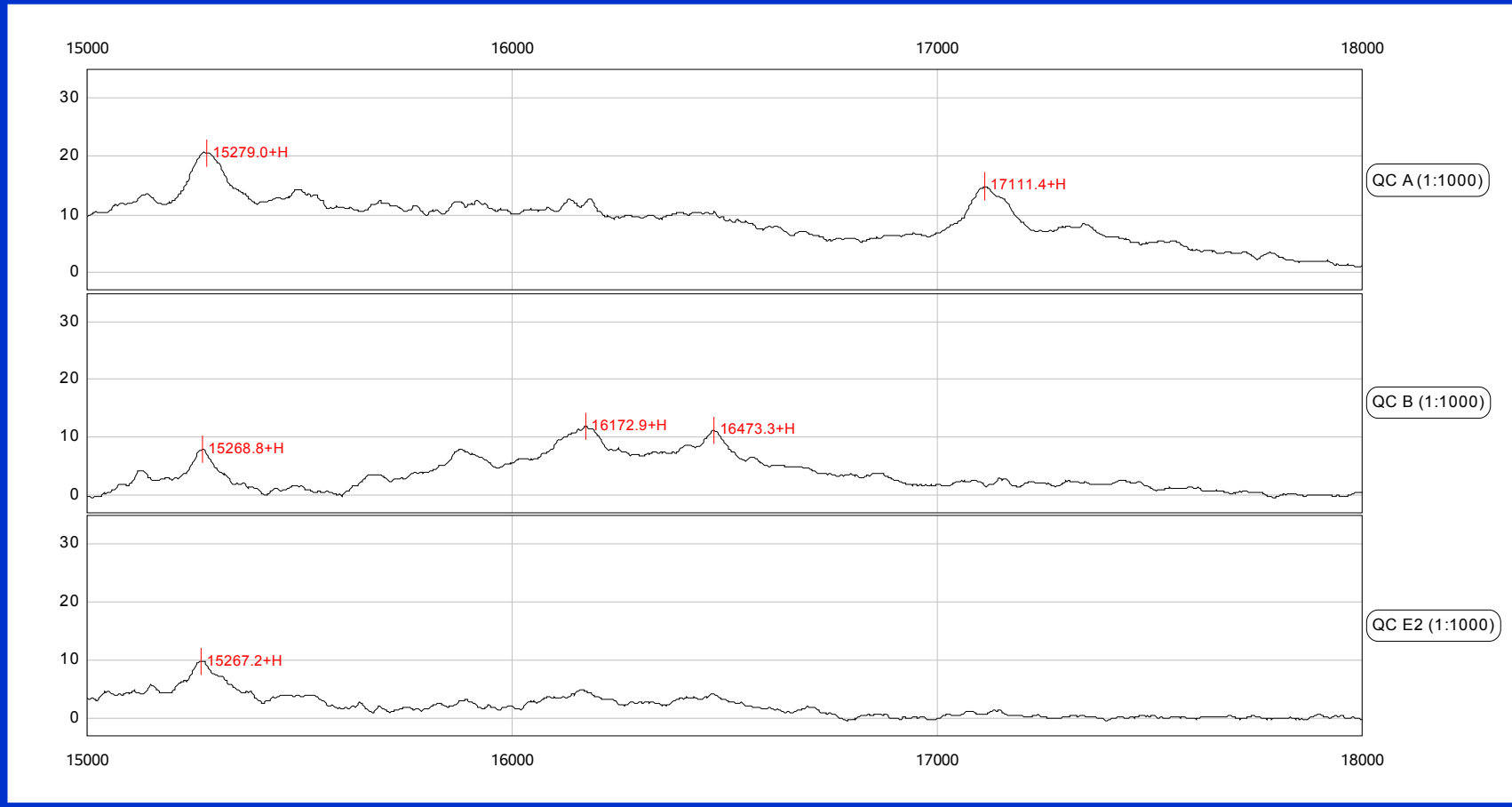


DAVD-DOF design

directional acceleration vector driven – displacement of fluids



Macro-results



Meaning …

TOFMS Spectrums Obtained Using the "*Direct Capture-In Situ Solubilization*" Technique For Purified Sub Strains of Salmonella (QC **A**, QC **B** and QC **E2**). All Sub-strains tested have a peak at a MW of~15, 270 including sub-strain E2. Only sub-strain A has an additional peak at~17, 110, whereas only sub-strain B has peaks at~16, 170 and ~16, 470. Signal associated with each sample of Salmonella sub-strain detected using this approach is associated with a maximum theoretical number of 1600 captured bacteria.

The end

Actual situation: waiting for the feedback from the measurements to be done at Houston to compare results and see whether or not the μ–device works.

Thank you !